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BY

H. P. BOWDITCH, M.D., Boston
R. H. CHITTENDEN, Ph.D., New Haven
W. H. HOWELL, M.D., Baltimore
FREDERIC S. LEE, Ph.D., New York
JACQUES LOEB, M.D., Chicago
W. P. LOMBARD, M.D., Ann Arbor
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THE INFLUENCE OF BORAX AND BORIC ACID UPON NUTRITION WITH SPECIAL REFERENCE TO PROTEID METABOLISM.

By R. H. CHITTENDEN and WILLIAM J. GIES.

[*From the Sheffield Laboratory of Physiological Chemistry, Yale University.*]

IN view of the wide-spread use of borax and boric acid as food preservatives it is somewhat singular that our knowledge of the influence of these substances upon the nutritional processes of the body is so slight and uncertain. E. de Cyon,[1] M. Gruber,[2] and J. Forster[3] have indeed studied the action of these agents upon proteid metabolism, but with results which are utterly lacking in harmony. Thus Cyon's work with borax seemingly indicates that proteid metabolism is diminished under its influence, *i. e.*, that borax tends to protect the consumption of proteid matter in the tissues. Gruber's experiments, on the other hand, indicate with equal positiveness that borax has no proteid sparing power, but really leads to an increase in the rate of proteid metabolism. To add to the uncertainty, the experiments with boric acid carried out under Forster's supervision tend to show that this agent is wholly without influence upon proteid metabolism. Obviously, conclusions which are so much at variance cannot be accepted without careful consideration.

[1] Cyon: Sur l'action physiologique du borax. Comptes rendus, 1878, tome 87, p. 845.

[2] Gruber: Ueber den Einfluss des Borax auf die Eiweisszersetzung im Organismus. Zeitschr. f. Biol., 1880, Band 16, p. 198.

[3] Forster: Ueber die Verwendbarkeit der Borsäure zur Conservirung von Nahrungsmitteln. Nach Versuchen von Dr. G. H. Schlencker aus Surakarta. Archiv. f. Hygiene, 1884, Band 2, p. 75.

Cyon's experiments were conducted simultaneously on three full-grown dogs which were fed upon a diet almost exclusively proteid. His observations were practically limited to determining changes in body-weight during short periods, with an estimation of the nitrogen of the urine. He found that during the period when borax was included in the food, the animals gained noticeably in body-weight and that less nitrogen was contained in the excreta than in the ingesta. From these very crude observations the conclusion was drawn that borax, even to the extent of 12 grams per day, may be ingested with the food, especially when the latter is essentially proteid in nature, without provoking the slightest disturbance in general nutrition. Further, Cyon appeared to see in his results evidence that borax, if substituted for common salt in food, will facilitate the assimilation of the latter and bring about a great increase in the weight of the animal. Such deductions, however, were wholly unwarranted from the data at hand, for not only were the periods of observation exceedingly short, but, as pointed out by both Gruber[1] and C. Voit,[2] the animals at the beginning were much emaciated and received throughout the experiment such excessive quantities of meat that increase of body-weight would have inevitably followed without the presence of borax. Consequently, all that can be inferred legitimately from Cyon's experiments is that assimilation and general metabolism were not seriously affected by borax in the quantities given.

In Gruber's work more scientific methods were pursued, but it may well be questioned whether the conditions under which the experiments were conducted were adapted for bringing out clearly the full action of borax upon proteid metabolism. The two dogs employed were fed simply upon meat and water, and were presumably in a condition of nitrogenous equilibrium. In the first experiment, where the animal received daily 1500 grams of meat and 200 c.c. of water, the daily excretion of urea in the urine varied from 75.82 grams to 110.30 grams during the six days prior to the administration of borax. Then 20 grams of borax were introduced with the food, an amount so large that vomiting was at once produced, leading to a loss of about 5 grams of the borax and about 100 grams of the meat, with most of the water. On this day, however, 108.20 grams of urea were excreted in the urine, although the food consumed was 100 grams less than the usual quantity. On the two fol-

[1] GRUBER: loc. cit.

[2] VOIT: Hermann's Handbuch der Physiologie, Band 6, Theil I, p. 165.

lowing days, without borax and with the full complement of food, the excretion of urea amounted to 109.00 and 107.00 grams respectively. From these results Gruber concludes that the borax increased the excretion of urea 4–6 per cent. In the second experiment, with a dog of 34 kilos body-weight, fed on a daily ration of 1100 grams of meat and 200 c.c. of water, the daily excretion of urea varied from 70.86 grams to 80.60 grams for the four days of the normal period, while the administration of 10 grams of borax was accompanied by an excretion of 82.14 grams of urea, and, on the second day following, the introduction of 20 grams of borax was accompanied by an excretion of 85.25 grams of urea. Further, on this latter day the volume of urine rose to 1310 c.c., while the largest daily excretion prior to this day was 1040 c.c. Gruber, therefore, concludes that borax does not spare proteid as Cyon asserts, but, just as in the case of common salt, sodium sulphate, and other neutral salts, it causes an increase in the elimination of water from the body and induces therewith an increased proteid catabolism. It is not to be inferred from this statement that there is simply an increased washing out of urea from the tissues, for, as Voit[1] has pointed out, the amounts of urea excreted on the days following the ingestion of borax simply fall back to the neighborhood of the average for the normal period, and do not drop below that average. Gruber also concludes that borax has no unfavorable influence upon the assimilation of food, since the quantity of fæces, their content of solid matter and of nitrogen are within the limits of the normal elimination during periods when meat alone is fed. Further, no harmful influence, even after the ingestion of the largest dose — 20 grams — was to be observed, and the appetite of the animal was found to be undiminished on the days following that upon which borax was given. The objection we would make to accepting Gruber's conclusions in their entirety is that they are based solely upon the results following the administration of two large doses of borax, 10 and 20 grams, whereas, to our mind, longer periods with a dosage of borax continued for several days in succession would seemingly render the conditions much more favorable for an accurate judgment as to the character of the influence exerted by the substance on tissue changes. Further, since urea alone was determined in the urine, possible minor changes connected with the presence of the salt would naturally be overlooked. Lastly, we are inclined to the view that it is extremely

[1] Voit: loc. cit. p. 165.

hazardous to draw such sweeping conclusions from one or two single experiments of this nature, especially where, as in the animal body, individual characteristics not infrequently give rise to exceptional results quite foreign to those ordinarily obtainable.

In Forster's work with boric acid, Dr. Schlencker experimented on himself, using a mixed diet and taking boric acid in daily doses of 1–3 grams. Each experiment consisted of three periods, of three days each, the boric acid being taken in the middle period. The conclusions arrived at were that proteid metabolism is not influenced, the excretion of urea in the boric-acid period being midway between that of the fore and after periods. It was noticed, however, that the quantity of ethereal sulphuric acid in the urine was considerably lessened in the boric-acid period and in the period following, thus implying an inhibitory influence upon the putrefactive processes of the intestine. Further, it was observed that the volume of the fæces, together with the contained nitrogen, was greatly increased under the influence of boric acid, from which it was inferred that this agent interferes with the assimilation of the food and perhaps, at the same time, gives rise to an increased secretion of mucus with a possible increase in the discharge of epithelial cells from the intestinal mucosa. This latter, however, is purely conjectural. Increased secretion of bile is also said to result from the action of boric acid. On the pulse and temperature no action was observed.

It is thus quite evident that the influence of borax and boric acid on nutrition, and especially their influence on proteid metabolism, is by no means wholly settled. The preceding statements clearly emphasize the uncertainty of our present information on the more essential features of the question before us, and we have therefore deemed it desirable to carry out, as thoroughly as possible, a series of experiments upon the action of both borax and boric acid on proteid metabolism and related phases of nutrition.

Conduct of the Experiments. — The experiments were conducted wholly upon full-grown dogs ranging in weight from 8 to 12 kilos. The animals were confined in suitable cages partially lined with galvanized iron and with the floor so arranged that both fluid and solid excreta could be collected in their entirety, while the upper portions of the cage were so constructed as to permit unrestricted circulation of air. In view of the length of the experiments — ranging from twenty-seven to fifty-six days each, with periods of eight to ten days duration — it seemed inadvisable as well as unnecessary to empty the

bladder each day with a catheter. Such diurnal variations as might possibly occur from incomplete emptying of the bladder at the end of the twenty-four hours would obviously be neutralized in periods of the above length, and consequently the urine was collected as naturally excreted, thus avoiding any possible disturbance of the normal condition of the bladder, etc. At the end of each twenty-four hours, the urine collected was combined, and its volume, specific gravity, etc., determined, after which the bottom of the cage was rinsed with a little distilled water and these washings added to the main fluid. The latter was then made up to some convenient volume in preparation for the daily analysis.

The fæces whenever passed were collected in a weighed dish, the mass thoroughly desiccated over a water-bath, and the dry weight ascertained. The dried material was then pulverized and the nitrogen-content as well as the ether-soluble matter determined in sample portions. The nitrogen determinations were always made in duplicate by the Kjeldahl method and rarely varied more than 0.05 per cent. Whenever, as sometimes occurred, hair accumulated in the cage it was likewise collected and the nitrogen determined. The ether-soluble matter was determined by extraction of the dried fæces in a Soxhlet-apparatus.

The animals were fed during the experiments on a mixed diet composed of fresh lean beef, cracker dust, lard, and water. The meat was prepared as follows: fresh lean beef, freed as far as possible from all adherent fat and connective tissue, was run through a hashing machine, after which it was enclosed in a bag of thin cloth, placed under a heavy press, and kept there under increasing pressure for several hours, the bloody fluid which drained off being thrown away. By this method there results a mass of tissue free from surplus moisture, and which, when enclosed in a bottle, will keep perfectly fresh on ice for seven to ten days without separation of fluid. Several advantages accrue from this method. Thus, we have a perfectly homogeneous mixture which can be drawn from for at least a week with surety that its nitrogen-content is constant. There is therefore no necessity for a daily determination of nitrogen in this portion of the diet, for each sample can be analyzed when prepared and the data accepted as long as the meat keeps fresh. Further, meat prepared in this manner at different times, if subjected to essentially the same pressure, varies only slightly in its content of nitrogen. We have invariably analyzed each lot when prepared to avoid any pos-

sibility of error, but, as the following results show, the differences in composition are very slight and necessitate very little alteration in the proportion of meat when changing from one lot to another. The following results are a few of the many obtained:

	Weight of Meat.	Absolute Content of Nitrogen.	Percentage of Nitrogen.
1.	0.8703 gram	0.03041 gram	3.49
	0.7710 "	.02682 "	3.48
	0.7631 "	.02628 "	3.44
2.	0.7673 gram	0.02716 gram	3.54
	0.9228 "	.03238 "	3.51
	1.0591 "	.03723 "	3.52
3.	0.8478 gram	0.03015 gram	3.56
	1.0014 "	.03591 "	3.59
	0.8876 "	.03152 "	3.55
4.	1.0082 gram	0.03642 gram	3.61
	1.0445 "	.03783 "	3.62
	1.0803 "	.03961 "	3.67
5.	1.1977 gram	0.04265 gram	3.56
	0.8142 "	.02902 "	3.56
	0.9793 "	.03463 "	3.54

The carbohydrate element in the diet, as already stated, was supplied by commercial cracker dust. This was purchased in large quantity and preserved in well stoppered bottles. It contained on an average 1.46 per cent of nitrogen. The lard employed was entirely free from any recognizable amount of nitrogen.

The daily diet was divided into two equal portions, one-half being fed at 8 A.M. and the other half at 6 P.M. When borax or boric acid was given, the daily dose was likewise divided and given either with the food or directly after. The body-weight of the animal was taken each morning just before feeding. Each day's urine included the fluid passed from 8 A.M. to 8 A.M. of the next day.

Methods of Analysis. — Nitrogen was determined wholly by the Kjeldahl method, viz., in the daily analyses of the urine, fæces, and food material. All analyses were made in duplicate, and the figures given are based upon the average of closely agreeing results. In analysis of the urine 5 c.c. were used for each determination, oxida-

tion being carried out in a long-necked Kjeldahl flask with 10 c.c. of sulphuric acid and a crystal of cupric sulphate, thus doing away with the necessity of adding sodium sulphide in the distillation. The ammonia formed was distilled into quarter-normal hydrochloric acid, the latter being titrated with quarter-normal ammonia, using congo red as an indicator.

Sulphur and phosphorus were determined in the customary manner by evaporating a given volume of the urine — 25 c.c. for each determination — in a roomy silver crucible with 10 grams of pure sodium hydroxide (made from the metal) and 2 grams of potassium nitrate, igniting the residue until oxidation was complete and treating the fused mass with water. For sulphur, the mixture was acidified with hydrochloric acid, evaporated to dryness, the residue moistened with a few drops of hydrochloric acid and dissolved in hot water. The filtered solution was then precipitated in the usual manner with barium chloride, the resultant barium sulphate filtered, ignited, and weighed, thus giving data for calculation of the total sulphur. For phosphorus, the aqueous extract of the oxidized urine was acidified with nitric acid, evaporated to dryness, the residue moistened with nitric acid and dissolved in warm water. From this solution the phosphoric acid was precipitated in the usual manner with molybdic solution and eventually transformed into ammonio-magnesium phosphate. From the weight of magnesium pyrophosphate obtained, the total phosphorus of the urine was calculated.

Uric acid was determined by the well-known Salkowski-Ludwig silver method, using 100–200 c.c. of urine.

Phosphoric acid was determined by Mercier's[1] modification of Neubauer's method, *i. e.* by titration of 50 c.c. of urine with a standard solution of uranium nitrate and tincture of cochineal as an indicator.

Total sulphuric acid was estimated by diluting 25 c.c. of urine with 3–4 volumes of water, adding 5 c.c. of dilute hydrochloric acid, heating to boiling, and precipitating hot with barium chloride. The barium sulphate so obtained, after standing twenty-four hours in a warm place, was washed with hot water until free from chlorides and lastly with hot alcohol, ignited, and weighed.

Combined sulphuric acid was determined by Baumann's method, using 100 c.c. of urine.[2]

[1] See Neubauer und Vogel's Analyse des Harns, neunte Auflage, p. 450.

[2] Ibid., p. 447.

Chlorine was determined in 10 c.c. of urine by Neubauer and Salkowski's modification of Mohr's method.[1] Other methods occasionally made use of are referred to in their appropriate place.

First Experiment. With Borax. — The animal made use of in this experiment was a short-haired mongrel bitch weighing about 12 kilos. She was brought into a condition approximating to nitrogenous equilibrium only after a preliminary period of nearly three weeks, during which time superfluous fat was lost and she became wholly accustomed to her surroundings. The daily food, at the time the experiment actually commenced, consisted of 250 grams of the prepared meat, 70 grams of cracker dust, 40 grams of lard, and 500 c.c. of water. It contained 9.814 grams of nitrogen. This diet, with the above content of nitrogen, was adhered to throughout the entire experiment of twenty-seven days, the only variation being the slight changes in the amount of nitrogen, to be seen in the tables, incidental to the use of different lots of meat and in the employment of gelatin capsules during the borax period. These gelatin capsules, in which the borax was administered, contained 14.95 per cent of nitrogen, the four capsules used each day during the borax period containing 0.12 gram of nitrogen. This amount was naturally included in the nitrogen of the food.

The experiment extended through twenty-seven days and was divided into three periods of nine days each: a fore or normal period during which no borax was given, a borax period during which 45 grams of borax (5 grams a day) were administered, and an after period when normal conditions again prevailed. During the borax period of nine days the quantity of borax given per day amounted to nearly 0.6 per cent of the total food and drink ingested, while of the solid food it formed 1.3 per cent. This dosage of borax, considering the size of the animal, was fairly large, and with this particular dog considerable difficulty was experienced in inducing the animal to take it. At first the borax was simply mixed with the food, but its presence was quickly detected and the food refused, although it was eventually coaxed down, but with some difficulty. After this first day the borax was given in capsules, as already stated, and no further difficulty of this sort was experienced. Three times during the borax period, however, the animal was nauseated and vomited a portion of the food, thus showing that this quantity of borax was sufficient to disturb the physiological equilibrium of the animal.

[1] See Neubauer und Vogel's Analyse des Harns, neunte Auflage, p. 437.

The vomited matter was eventually eaten, however, later in the day, so that this occurrence did not disturb the validity of the experiment. It will be remembered that in Gruber's experiment with a much larger dog (39 kilos) 20 grams of borax likewise caused vomiting. In his experiment, however, the entire dose of borax was taken at one time, while in our case, 2.5 grams were given in the morning and a like quantity at night. Hence, taking into account the weight of the dog, it might perhaps be argued that 0.25 gram of borax to 1 kilo of body-weight will produce vomiting. This, however, is very questionable, for in the above experiment the dog did not vomit until the afternoon of December 5, when she had already taken 12.5 grams of borax. In other words, the animal was without doubt suffering in part from the cumulative action of the salt. Thus, there was a slight attack of vomiting again on the fifth day (December 7) and a final attack on the eighth day (December 10). During the after period of nine days the animal was perfectly normal, and at the close of the period, to again test the action of the borax, 5 grams were given at one time shortly after the morning meal. Forty-five minutes afterwards the animal vomited, and this occurred three times during the forenoon. We are inclined to lay particular emphasis upon this action of the borax because it tends to show that in this first experiment the dosage of borax through the nine days' period was as large as it well could be for this particular animal without vitiating the experiment, and that the conditions were therefore well adapted for bringing out distinctly any possible influence the borax might have upon the metabolic phenomena of the body. Further, we would call attention to the obvious advantage — in spite of the greater labor involved — of continuing experiments of this character over comparatively long periods of time. To be sure, in some cases where the substance being tested has a marked physiological action, a single dose may show at once the character of the influence exerted, but too often erroneous conclusions are arrived at through negligence of this precaution. Where, however, the substance under examination is given for five to ten days consecutively, with careful examination of the excreta, the chances of detecting minor influences are greatly increased, and at the same time the danger of being led astray by a single exceptional result — or by other possible errors — is greatly diminished.

The following tables contain the analytical results obtained throughout the experiment.

FIRST EXPERIMENT. — FORE PERIOD.

Date.	Body.	Food.	Urine.									Fæces.	
1896. Nov.	Weight.	Nitrogen.	Vol.	Sp. gr.	Reaction.	Nitrogen.	Uric Acid.	Phosphorus.	Sulphur.	Total SO_3.	Combined SO_3.	Dry Weight.	Nitrogen.
	kilos	grams	c.c.		litmus	grams							
24	10.9	9.814	505	1018	Acid.	7.945	0.038	0.468	0.491	0.962	0.058	....	....
25	10.9	9.814	716	1018	"	11.361	.049	.646	.720	1.388	.075	....	....
26	10.9	9.814	773	1017	"	11.367	.061	.688	.671	1.343	.077	....	....
27	11.0	9.814	786	1016	"	12.476	.049	.763	.737	1.521	.084	....	....
28	11.0	9.814	650	1017	"	10.069	.047	.585	.586	1.214	.064	....	....
29	11.0	9.814	415	1017	"	6.102	.040	.325	.381	0.765	.032	....	....
30	10.8	9.814	770	1019	"	12.302	.066	.760	.758	1.554	.084	....	....
Dec. 1	10.9	9.814	575	1017	"	8.995	.040	.505	.570	1.148	.062	....	....
2	11.0	9.814	439	1018	"	6.568	.038	.410	.405	0.804	.055	38.15	2.122
				Nitrogen of Urine = 87.185 Nitrogen of Fæces = 2.122									
Totals . . .		88.326	5629			89.307	0.428	5.150	5.319	10.699	0.591	38.15	2.122
Daily Averages		9.814	625			9.923	0.048	0.572	0.591	1.189	0.066		0.236

FIRST EXPERIMENT. — BORAX PERIOD.

Date.	Body.	Food.	Borax.	Urine.									Faces	
1896. Dec.	Weight.	Nitrogen.		Vol.	Sp. gr.	Reaction.	Nitrogen.	Uric Acid.	Phosphorus.	Sulphur.	Total SO_3.	Combined SO_3.	Dry Weight.	Nitrogen.
	kilos	grams		c.c.		litmus	grams							
3	10.9	9.903	5	796	1021	Acid.	13.344	0.054	0.821	0.789	1.631	0.097	....	....
4	11.1	9.933	5	368	1022	Alkaline.	5.909	.032	.321	.371	0.705	.039	....	....
5	11.2	9.933	5	485	1025	"	9.183	.039	.535	.527	1.103	.057	....	....
6	11.1	9.933	5	520	1027	"	10.043	.042	.568	.592	1.197	.060	....	....
7	11.1	10.016	5	686	1024	"	12.823	.050	.818	.754	1.526	.068	35.91	2.292
8	11.2	10.100	5	422	1024	"	7.412	.051	.444	.426	0.825	.042	....	....
9	11.2	10.100	5	604	1023	"	10.742	.049	.615	.596	1.228	.069	....	....
10	11.3	10.100	5	498	1026	"	9.846	.031	.521	.600	1.174	.060	....	....
11	11.3	10.100	5	602	1020	"	8.825	.063	.456	.554	1.040	.063	24.68	1.627
					Nitrogen of Urine = 88.127 Nitrogen of Fæces = 3.919									
Totals . . .		90.118	45	4981			92.046	0.411	5.099	5.209	10.429	0.555	60.59	3.919
Daily Averages		10.013	5	553			10.227	0.046	0.567	0.579	1.159	0.062		0.435

FIRST EXPERIMENT.—AFTER PERIOD.

Date	Body.	Food.	Urine.									Fæces.	
1896. Dec.	Weight	Nitrogen	Vol.	Sp. gr.	Reaction.	Nitrogen.	Uric Acid.	Phosphorus.	Sulphur.	Total SO_3.	Combined SO_3.	Dry Weight	Nitrogen.
	kilos	grams	c.c.		litmus	grams							
12	11.5	9.981	488	1019	Acid.	8.727	0.042	0.441	0.596	1.024	0.055	....	....
13	11.3	9.981	670	1018	"	10.632	.053	.589	.716	1.247	.073	....	....
14	11.4	9.981	691	1017	"	10.047	.039	.621	.742	1.265	.083	....	....
15	11.5	9.981	551	1016	"	7.804	.032	.482	.601	0.978	.049	....	....
16	11.4	9.981	681	1018	"	10.549	.051	.694	.736	1.345	.073	33.25	1.995
17	11.5	9.981	595	1019	"	10.121	.036	.662	.662	1.213	.062	....	....
18	11.5	9.981	572	1018	"	9.232	.036	.587	.613	1.119	.069	....	....
19	11.5	9.981	630	1017	"	9.587	.056	.574	.610	1.083	.068	....	....
20	11.5	10.036	549	1019	"	9.678	.044	.574	.616	1.180	.069	25.45	1.629
				Nitrogen of Urine = 86.377 Nitrogen of Fæces = 3.624									
Totals . . .		89.884	5427			90.001	0.389	5.224	5.892	10.454	0.601	58.70	3.624
Daily Averages		9.987	603			10.000	0.043	0.580	0.655	1.162	0.067		0.403

FIRST EXPERIMENT. — GENERAL SUMMARY.

Periods.	Total Nitrogen.			Urine.							Fæces.	
	Ingested.	Excreted.	Balance.	Vol.	Nitrogen.	Uric Acid.	Phosphorus.	Sulphur.	Total SO_3.	Combined SO_3.	Dry Weight	Nitrogen.
	grams			c.c.	grams							
Fore	88.326	89.307	−0.981	5629	87.185	0.428	5.150	5.319	10.699	0.591	38.15	2.122
Borax	90.118	92.046	−1.928	4981	88.127	.411	5.099	5.209	10.429	.555	60.59	3.919
After	89.884	90.001	−0.117	5427	86.377	.389	5.224	5.892	10.454	.601	58.70	3.624

Referring now to the tables containing the results of the first experiment, it is to be noted that in the fore period of nine days the total nitrogen ingested amounted to 88.326 grams, while in the urine excreted during this period there were contained 87.185 grams of nitrogen, and in the fæces 2.122 grams, making a total of 89.307 grams of nitrogen; hence the nitrogen balance for the period of nine days is —0.981 gram. The body-weight remained practically constant. The slight excess of nitrogen excreted over the amount ingested in this period is due possibly to lack of complete involution of the mammary glands[1]; the deficiency, however, is too slight, considering the length of the period, to need much consideration. For comparison, the results of the three periods, showing the relative excretion of nitrogen, may be arranged in tabular form:

	Fore Period.		*Borax Period.*		*After Period.*	
Nitrogen of Food	88.326		90.118		89.884	
Nitrogen of Urine	87.185	89.307	88.127	92.046	86.377	90.001
Nitrogen of Fæces	2.122		3.919		3.624	
Nitrogen Balance	—0.981		—1.928		—0.117	
Ratio of Urine Nitrogen to Food Nitrogen	98.6 per cent.		97.7 per cent.		96.0 per cent.	

It is thus evident that in this experiment, in spite of the large doses of borax and the length of the period, proteid metabolism is not modified in any noticeable degree. The amount of nitrogen eliminated through the urine in proportion to the nitrogen of the food, during the borax period, differs from that of the fore period only to a slight extent, and this difference is due apparently to a diminished assimilation of the proteid food. The change in the nitrogen balance of the borax period is plainly caused by a slight increase in the amount of fæcal nitrogen, and not to increased metabolism, thus indicating that the borax has a tendency to diminish somewhat the absorption of proteid food, or possibly leads to an increased secretion of mucus. When, however, the nitrogen of the fæces of the borax period is compared with both that of the fore and after periods the increase is seen to be so slight that it is perhaps unwise to attach much importance to it. Certainly the borax, though given in doses sufficiently large to keep the animal on the verge of nausea, did not in this experiment interfere greatly with the

[1] MARCUSE: Ueber den Nährwerth des Caseins, Pflüger's Archiv. f. d. ges. Physiol., 1896, Band 64. p. 223.

digestion of any of the food-stuffs, since the fæces of the borax period are not much greater in amount than those of the after period, though somewhat larger than those of the fore period.

The weight of the animal during the twenty-seven days' period showed a tendency to rise somewhat, *i. e.*, from 10.9 kilos to 11.5 kilos. This, however, is not to be attributed to a laying on of fat nor to a retention of nitrogenous matter by the body, but is the result simply of a diminished excretion of water due to the presence of the borax. The results in this connection are in direct opposition to those obtained by Gruber with single doses of borax. There is here no suggestion whatever of an increased excretion of water, but on the contrary, a very marked decrease. Thus, by reference to the accompanying tables, it will be observed that during the fore period the total volume of urine excreted amounted to 5629 c.c. and the body-weight remained practically constant, *i. e.*, 10.9–11.0 kilos. During the borax period, however, the volume of urine excreted fell to 4981 c.c. and the body-weight gradually rose to 11.3 kilos, while in the after period the volume of urine rose to 5427 c.c. with a constant body-weight of 11.5 kilos. It is thus quite clear that borax may decidedly check the output of water through the kidneys, and lead, as in this case, to its retention within the body.

Very noticeable also, in this experiment, is the sudden change in the specific gravity of the urine, as also in the reaction of the fluid, when borax is given. Thus, in the fore period the specific gravity of the urine stood at 1017–1018, but at the opening of the borax period it rose at once to 1022–1027, dropping back, however, as the borax was discontinued. Similarly, the reaction of the normal urine was acid to litmus, but on exhibition of borax, the reaction quickly changed to alkaline. The marked rise in the specific gravity of the urine during the borax period is not due solely to diminished elimination of water nor to increase in the proportion of metabolic products, but mainly to the borax itself, which is rapidly eliminated through the urine. We have not made any special trial to ascertain how soon the borax appears in the urine after its administration, but we have observed that the urine collected on the first day of the borax period gives, after acidulation with hydrochloric acid, a strong reaction with turmeric paper for boric acid. Further, that the elimination of borax through the urine is very rapid is manifest from the fact that, at the end of the borax period, the animal having received 45 grams of the salt, no trace of a reaction could be obtained with

turmeric paper on the *second* day of the after period. In other words, elimination of the borax was practically complete twenty-four to thirty-six hours after the last dose had been taken. These observations accord with Johnson's statements[1] that borax and boric acid begin to be eliminated through the urine a short time after their administration.

While it is clear from a study of the nitrogen excretion that proteid metabolism, under the conditions of this experiment, is not materially affected by borax, the other analytical results must not be overlooked. Thus, in the borax period the excretion of phosphorus, sulphur, total sulphuric acid, and combined sulphuric acid is slightly below that of the fore and after periods. The differences, however, are so small that it is perhaps unwise to draw any positive conclusions from them, other than to admit their negative character. It can certainly be asserted with perfect safety that the borax has failed to exert any marked influence upon the excretion of either sulphur or phosphorus. In this connection it will be remembered that Forster[2] found, on feeding boric acid to man, a marked increase in the output of phosphoric acid. Borax, however, certainly fails to produce any such result, its presence in the body (of the dog) tending on the other hand to reduce the output of phosphorus. Further, it is evident that the slight diminution in the excretion of combined sulphuric acid is not sufficient to indicate any inhibitory influence upon intestinal putrefaction. Lastly, the figures obtained in connection with uric acid are such as to indicate a purely negative action.

Second Experiment. With Boric Acid. — The animal experimented on was a short-haired mongrel bitch weighing 8 kilos. Nitrogenous equilibrium was quickly established on a daily diet composed of 160 grams of the prepared meat, 40 grams of cracker dust, 30 grams of lard, and 400 c.c. of water. This diet contained 6.144 grams of nitrogen and was practically adhered to throughout the experiment. The latter was of thirty days' duration, *i. e.*, three periods of ten days each. During the middle, or boric acid period, 1–2 grams of boric acid were given daily mixed with the food, the animal taking it without

[1] JOHNSON: Ueber die Ausscheidung von Borsäure und Borax aus dem menschlichen Organismus. Jahresbericht f. Thierchemie, 1885, p. 235. See also, VIGIER: Note préliminaire sur l'action physiologique du borate de soude. Comptes rendus soc. de Biol. Paris, 1883, p. 44.

[2] FORSTER: Archiv. f. Hygiene, 1884, Band 2, p. 75.

the slightest reluctance and without any apparent effect upon the appetite. No sign of nausea or vomiting was seen. With 2 grams of boric acid per day the mixture of food and drink contained 0.31 per cent, while the dry food contained 0.86 per cent of boric acid. The total amount of boric acid given during the ten days was 14.5 grams.

During the fore period of ten days the animal received a total of 61.440 grams of nitrogen. The nitrogen excreted through the urine for this period amounted to 58.119 grams, while the fæces contained 3.203 grams, thus making a total of 61.322 grams of nitrogen excreted, with a nitrogen balance of +0.118 gram. Plainly, the animal was in a condition of nitrogenous equilibrium.

The relative excretion of nitrogen for the three periods may be seen in the following table:

	Fore Period.		*Boric Acid Period.*		*After Period.*	
Nitrogen of Food	61.440		62.032		61.943	
Nitrogen of Urine	58.119	61.322	59.600	63.538	58.979	62.923
Nitrogen of Fæces	3.203		3.938		3.944	
Nitrogen Balance . . .	+ 0.118		— 1.506		— 0.980	
Ratio of Urine Nitrogen to Food Nitrogen	94.5 per cent.		96.7 per cent.		95.2 per cent.	

From these figures it would appear that there is a slight tendency toward stimulation of proteid metabolism. When it is remembered, however, that the nitrogen balance for the boric acid period, —1.506, is the result of ten days' consecutive feeding with boric acid, it is manifest that the stimulating action is very slight, and our results may perhaps be considered as practically in accord with those reported by Forster, who found that in man on a mixed diet, boric acid in moderate doses (1–3 grams) was without influence on proteid decomposition as measured by the excretion of urea. Upon the assimilation of the proteid food there is no evidence of any action, *i. e.*, the nitrogen content of the fæces during the boric acid period is essentially the same as that of the fore and after periods. Further, the total weight of fæces for each of the three periods is so nearly the same, it is quite evident that assimilation has not been materially interfered with. In this respect our results fail to agree with those reported by Forster, who found that small doses of boric acid (1 gram in two days) given to a man on a mixed diet, and on a milk and egg diet, increased the excretion of fæces; this increase being due,

according to Forster, not to any decrease in the assimilation of fat nor to increase in the volume of the secretions, but to a decreased assimilation of the proteid food under the influence of the boric acid. This difference in our results may of course depend upon the difference in the character of the animal species. In our experiment, the weight of the animal remained perfectly constant throughout the entire period of thirty days.

The accompanying tables contain the various data obtained.

Unlike borax, boric acid fails to produce any change in the volume of the urine. Thus, in the fore period of ten days the total volume excreted amounted to 4647 c.c., while in the boric acid period of the same length the total volume was 4665 c.c., and in the after period 4644 c.c. Further, there is no marked difference, to be measured by litmus paper, in the reaction of the fluid, although, as the tables show, alkaline reaction is more common in the normal periods than in the boric acid period. In the latter period, however, the specific gravity of the urine, as might be expected, shows a higher average than in the two normal periods. This is due, as in the case of borax, to the rapid elimination of the boric acid through the urine. The latter shows the presence of the acid by the turmeric test on the first day of the boric acid period, while on the second day of the after period all trace of a reaction disappears, thus showing that the acid is rapidly eliminated from the body and is practically completely removed twenty-four to thirty-six hours after the last dose.

Upon the elimination of uric acid, boric acid appears to have a slight inhibitory effect, at least under the conditions of this experiment, but upon the excretion of total and combined sulphuric acid, chlorine and phosphoric acid, no tangible effect is produced. Certainly, the results in connection with combined sulphuric acid do not indicate any retarding effect upon the putrefactive processes of the intestine. In this connection it will be remembered that in Forster's experiments on man doses of boric acid, corresponding to those used by us, apparently gave rise to a marked retardation in the amount of ethereal sulphate excreted. As a result, Forster arrived at the conclusion that boric acid materially reduces intestinal putrefaction. Our results, however, show no action of this kind in the dog, and we are inclined to the view that both borax and boric acid are too rapidly eliminated from the system to be very effective in the intestine. As already stated, the elimination of borax and boric acid through the

SECOND EXPERIMENT. — FORE PERIOD.

Date.	Body.	Food.	Urine.									Faces.	
1897.	Weight.	Nitrogen.	Vol.	Sp. gr.	Reaction.	Nitrogen.	Uric Acid.	Total SO_3.	Combined SO_3.	Chlorine.	Total P_2O_5.	Dry Weight.	Nitrogen.
Feb.	kilos	grams	c.c.		litmus	grams							
24	7.9	6.144	500	1015	Acid.	6.642	0.037	0.682	0.023	0.354	0.950	....	....
25	7.9	6.144	486	1012	"	5.051	.055	.533	.021	.404	0.726	....	....
26	7.9	6.144	460	1014	"	5.741	.048	.638	.029	.340	0.789	6.96	0.450
27	8.0	6.144	410	1015	"	4.956	.049	.560	.024	.379	0.665	....	....
28	7.9	6.144	581	1014	"	7.605	.096	.830	.036	.573	1.053	....	....
Mar. 1	8.0	6.144	325	1014	"	4.067	.033	.477	.020	.210	0.506	....	....
2	7.9	6.144	525	1016	Alkaline.	7.613	.052	.807	.040	.404	1.008	11.90	0.780
3	7.9	6.144	440	1014	"	5.425	.057	.581	.022	.407	0.722	10.50	0.657
4	8.0	6.144	370	1014	"	4.119	.026	.464	.016	.291	0.540	....	....
5	7.9	6.144	550	1015	Acid.	6.900	.051	.749	.026	.462	1.004	17.30	1.316
				Nitrogen of Urine = 58.119 Nitrogen of Fæces = 3.203									
Totals . . .		61.440	4647			61.322	0.504	6.321	0.257	3.824	7.963	46.66	3.203
Daily Averages		6.144	465			6.132	0.050	0.632	0.026	0.382	0.796		0.320

SECOND EXPERIMENT. — BORIC ACID PERIOD.

Date.	Body.	Food.	Boric Acid.	Urine.									Faeces.	
1897. Mar.	Weight.	Nitrogen.		Vol.	Sp. gr.	Reaction.	Nitrogen.	Uric Acid.	Total SO_3.	Combined SO_3.	Chlorine.	Total P_2O_5.	Dry Weight.	Nitrogen.
	kilos	grams		c.c.		litmus	grams							
6	79	6.144	1	470	1016	Acid.	5.915	0.040	0.678	0.025	0.347	0.911	....	....
7	79	6.144	1	505	1016	"	6.390	.031	.712	.032	.451	0.946	....	....
8	80	6.183	1	380	1014	"	4.479	.028	.511	.020	.259	0.550	10.20	0.710
9	79	6.223	1	525	1017	"	7.280	.041	.767	.034	.356	1.073	....	....
10	80	6.223	1.5	400	1016	Alkaline.	4.166	.026	.481	.017	.333	0.586	9.75	0.660
11	79	6.223	1.5	530	1017	Acid.	7.460	.062	.803	.034	.555	1.017	....	....
12	79	6.223	1.5	460	1017	"	6.000	.040	.664	.031	.538	0.849	16.30	1.317
13	79	6.223	2	470	1017	"	6.035	.041	.682	.031	.565	0.841	....	....
14	79	6.223	2	480	1017	"	6.032	.035	.648	.027	.488	0.828	11.60	0.882
15	79	6.223	2	445	1017	"	5.843	.042	.683	.027	.425	0.899	5.45	0.369
					Nitrogen of Urine = 59.600 Nitrogen of Fæces = 3.938									
Totals . . .		62.032	14.5	4665			63.538	0.386	6.629	0.278	4.317	8.500	53.30	3.938
Daily Averages		6.203	1.45	467			6.354	0.039	0.663	0.028	0.432	0.850		0.394

SECOND EXPERIMENT.—AFTER PERIOD.

Date.	Body.	Food.	Urine.									Faeces.	
1897.	Weight.	Nitrogen.	Vol.	Sp. gr.	Reaction.	Nitrogen.	Uric Acid.	Total SO_3.	Combined SO_3.	Chlorine.	Total P_2O_5.	Dry Weight.	Nitrogen.
Mar.	kilos	grams	c.c.		litmus	grams							
16	7.9	6.223	432	1016	Acid.	6.100	0.057	0.670	0.026	0.346	0.813	5.45	0.369
17	8.0	6.223	360	1014	Alkaline.	4.318	.028	.526	.020	.226	0.526	7.71	.476
18	7.9	6.223	560	1016	"	7.630	.096	.874	.048	.604	1.106	....	....
19	7.9	6.223	485	1015	Acid.	6.284	.052	.717	.033	.448	0.890	8.82	.655
20	8.0	6.223	425	1013	Alkaline.	4.412	.040	.514	.023	.366	0.674	....	....
21	7.9	6.223	560	1017	Acid.	7.947	.069	.937	.053	.742	1.205	12.25	.814
22	7.9	6.041	490	1015	Alkaline.	5.922	.044	.678	.033	.528	0.831	....	....
23	7.9	6.188	450	1015	"	4.940	.036	.575	.022	.416	0.739	10.47	.798
24	7.9	6.188	480	1016	"	6.827	.037	.749	.038	.296	0.979	....	....
25	7.9	6.188	402	1015	"	4.599	.049	.571	.020	.260	0.686	10.90	.832
					Nitrogen of Urine	58.979							
					Nitrogen of Faeces	3.944							
Totals . . .		61.943	4644			62.923	0.508	6.811	0.316	4.232	8.449	55.60	3.944
Daily Averages		6.194	464			6.292	0.051	0.681	0.032	0.423	0.845		0.394

SECOND EXPERIMENT.—GENERAL SUMMARY.

Periods.	Total Nitrogen.			Urine.							Faces.	
	Ingested.	Excreted.	Balance.	Vol.	Nitrogen.	Uric Acid.	Total SO_3.	Combined SO_3.	Chlorine	Total P_2O_5.	Dry Weight.	Nitrogen.
	grams			c.c.	grams							
Fore . . .	61.440	61.322	+ 0.118	4647	58.119	0.504	6.321	0.257	3.824	7.963	46.66	3.203
Boric Acid .	62.032	63.538	— 1.506	4665	59.600	.386	6.629	.278	4.317	8.500	53.30	3.938
After . . .	61.943	62.923	— 0.980	4644	58.979	.508	6.811	.316	4.232	8.449	55.60	3.944

urine commences almost immediately after their ingestion, and it is very questionable, therefore, whether, with moderate doses of these substances, enough would remain unabsorbed at the lower end of the small intestine to exert much influence upon the growth and development of micro-organisms. Certainly, the fæces do not ordinarily contain any appreciable amount of borax or boric acid after these substances have been administered in moderate quantities, although obviously the length of time the fæces are forming will have some influence upon their content of soluble matter. In only one instance, to be detailed later, where a very large dose of borax was given, could any decided reaction for boric acid be obtained in the fæces. Johnson[1] states that in the case of the human organism borax and boric acid show great irregularity in their appearance in the fæces, and that he was able to detect them in the latter only in six cases out of fourteen, although daily doses of 0.9–3.0 grams of boric acid were given.

Lastly, it is to be noted that in our experiment with boric acid there is no such increase in the excretion of phosphoric acid through the urine as was observed by Forster; our results, indeed, fail to show any distinct influence exerted by boric acid upon the metabolism of phosphorized matter.

Third Experiment. With Borax and Boric Acid.— This experiment was divided into seven periods of eight days each, thus making a total of fifty-six consecutive days during which the variations in the composition of the urine and fæces were followed as before, under the influence of both borax and boric acid. The object in extending the experiment through this lengthy period was to ascertain whether prolonged treatment with borax and boric acid might not eventually result in such a disturbance of physiological equilibrium that more positive data would be obtained. With this end in view, a mongrel bitch of ten kilos body-weight was brought into nitrogenous equilibrium, after which the urine and fæces were analyzed for eight consecutive days, *i. e.*, the fore period. Borax was then given with the food for eight days, making the first borax period. This was followed by another period of eight days during which neither borax nor boric acid were administered, after which came a third period of eight days when boric acid was fed. This, in turn, was succeeded by a normal period of equal length, followed by eight days of borax treatment —

[1] Johnson: Ueber die Ausscheidung von Borsäure und Borax aus dem menschlichen Organismus. Jahresbericht f. Thierchemie, 1885, p. 235.

the second borax period — concluding with a final after period of eight days, *i. e.*, a total of fifty-six days. By thus keeping the same animal under continuous observation for this length of time it might reasonably be expected that any cumulative action — assuming it to exist — would be clearly manifest. Further, considerably larger daily doses of borax and boric acid were administered than in the preceding experiments.

The daily diet made use of throughout the entire experiment consisted of 160 grams of the prepared meat, 40 grams of cracker dust, 30 grams of lard, and 430 c.c. of water. Its exact content of nitrogen is shown in the table of the fore period. The total amount of nitrogen ingested during the fore period was 52.163 grams. The amount excreted during the same period was 51.734 grams, thus showing a nitrogen balance for the eight normal days of +0.429 grams. The dog used in this experiment, although short-haired, lost considerable hair daily. This was therefore collected and at the end of each period its content of nitrogen was determined and the amount added to the nitrogen of the urine and fæces, as seen in the accompanying tables. It is interesting to note in this connection that the loss of hair in periods of eight days' duration may be considerable; so large, indeed, that an appreciable loss of nitrogen may result. Thus, in the seven periods of this experiment the total amount of hair shed was 61.98 grams, *i. e.*, 8–10 grams for each period, the total nitrogen thrown off in this manner amounting to 7.856 grams. These figures show that the hair shed contained 12.6 per cent of nitrogen. Obviously, in careful experiments, this source of loss cannot be overlooked.

In the first borax period of eight days the daily dose of borax ranged from 2 to 5 grams, the total amount administered being 32.5 grams. In the following boric acid period the daily dose ranged from 1 to 3 grams, a total of 17 grams of boric acid being given. On commencing the second borax period the daily dose of borax was placed at 10 grams. This was continued for two days, but on the third day after taking the morning dose of 5 grams the animal's appetite began to fail so that it became necessary to coax her considerably in order to have the day's ration consumed. On this day, therefore, only 5 grams were given, but on the following day the appetite was nearly normal and 6 grams of borax were given. The dose was then raised to 10 and 8 grams daily, as shown in the tables, a total of 64 grams of borax being given in this period of eight days.

THIRD EXPERIMENT. — FORE PERIOD.

Date.	Body.	Food.	Urine.								Feces.	
1897. April.	Weight.	Nitrogen.	Vol.	Sp. gr.	Reaction.	Nitrogen.	Uric Acid.	Total SO_3.	Combined SO_3.	Total P_2O_5.	Dry Weight.	Nitrogen.
	kilos	grams	c.c.		litmus	grams						
21	10.0	6.593	490	1015	Acid.	6.160	0.040	0.525	0.042	0.981	....	....
22	10.0	6.770	470	1013	"	5.050	.032	.437	.036	0.697	....	....
23	10.0	6.770	540	1016	"	7.139	.042	.641	.071	1.117	....	....
24	10.1	6.406	440	1014	"	5.231	.028	.489	.059	0.779	....	....
25	10.0	6.406	640	1015	"	7.685	.000	.746	.093	1.329	14.33	0.846
26	10.0	6.406	465	1012	"	4.643	.031	.420	.039	0.638	....	....
27	10.0	6.406	525	1014	"	5.641	.047	.544	.061	0.862	....	....
28	9.9	6.406	626	1015	"	7.544	.035	.713	.094	1.335	10.36	0.571
				Nitrogen of Urine = 49.093 Nitrogen of Fæces = 1.417 Nitrogen of Hair = 1.224								
Totals . . .		52.163	4196			51.734	0.315	4.515	0.495	7.738	24.69	1.417
Daily Averages		6.520	525			6.467	0.039	0.564	0.062	0.967		0.177

THIRD EXPERIMENT. — FIRST BORAX PERIOD.

Date.	Body.	Food.	Borax.	Urine.								Fæces.	
1897. April.	Weight.	Nitrogen.		Vol.	Sp. gr.	Reaction.	Nitrogen.	Uric Acid.	Total SO_3.	Combined SO_3.	Total P_2O_5.	Dry Weight.	Nitrogen.
	kilos	grams		c.c.		litmus	grams						
29	10.0	6.406	2	400	1015	Alkaline.	4.025	0.039	0.401	0.049	0.597	2.96	0.163
30	10.1	6.406	3	400	1022	"	6.738	.043	.677	.091	1.142	....	....
May 1	10.0	6.406	4	591	1018	"	6.542	.042	.704	.089	1.107	....	....
2	10.0	6.406	4	470	1021	"	7.028	.042	.797	.126	1.089	....	....
3	9.9	6.406	4.5	520	1017	"	5.916	.031	.565	.072	0.781	20.10	0.990
4	10.1	6.285	5	380	1017	"	4.041	.024	.372	.040	0.409	....	....
5	10.1	6.285	5	460	1022	"	6.531	.040	.597	.082	0.977	....	....
6	10.0	6.285	5	540	1022	"	7.503	.032	.792	.113	1.272	20.69	1.023
					Nitrogen of Urine = 48.324 Nitrogen of Fæces = 2.176 Nitrogen of Hair = 1.186								
Totals . . .		70.885	32.5	3761			51.686	0.293	4.905	0.662	7.374	43.75	2.176
Daily Averages		6.361	4.06	470			6.461	0.037	0.613	0.083	0.922		0.272

THIRD EXPERIMENT.— FIRST AFTER PERIOD.

Date.	Body.	Food.	Urine.								Faeces.	
1897: May.	Weight.	Nitrogen.	Vol.	Sp. gr.	Reaction.	Nitrogen.	Uric Acid.	Total SO_3.	Combined SO_3.	Total P_2O_5.	Dry Weight.	Nitrogen.
	kilos	grams	c.c.		litmus	grams						
7	10.1	6.285	410	1015	Acid.	5.687	0.036	0.575	0.054	0.810	....	....
8	10.2	6.285	430	1012	"	4.330	.034	.449	.040	0.458	....	....
9	10.1	6.285	590	1016	"	7.671	.044	.623	.117	1.187	....	....
10	10.2	6.428	390	1014	"	4.717	.014	.563	.065	0.599	....	....
11	10.0	6.428	597	1015	"	7.425	.036	.872	.106	1.423	19.55	0.745
12	10.0	6.428	530	1013	"	5.952	.029	.586	.060	1.066	....	....
13	10.1	6.428	525	1014	"	5.894	.029	.620	.065	1.017	11.90	.627
14	10.1	6.428	490	1013	"	5.754	.026	.568	.055	0.959	8.21	.473
				Nitrogen of Urine = 47.430 Nitrogen of Faeces = 1.845 Nitrogen of Hair = 1.059								
Totals . . .		50.595	3962			50.334	0.248	4.856	0.562	7.519	39.66	1.845
Daily Averages		6.374	495			6.292	0.031	0.607	0.070	0.940		0.231

THIRD EXPERIMENT. — BORIC ACID PERIOD.

Date 1897. May.	Body. Weight.	Food. Nitrogen.	Boric Acid.	Urine. Vol.	Sp. gr.	Reaction.	Nitrogen.	Uric Acid.	Total SO_3.	Combined SO_3.	Total P_2O_5.	Faeces. Dry Weight.	Nitrogen.
	kilos	grams		c.c.		litmus	grams						
15	10.1	6.428	1	525	1015	Acid.	5.677	0.039	0.558	0.068	1.003	2.73	0.157
16	10.1	6.396	1	441	1015	"	5.424	.035	.627	.066	0.785	....	....
17	10.2	6.396	1.5	401	1014	"	4.247	.053	.454	.038	0.502	....	....
18	10.2	6.396	2	490	1015	"	5.909	.018	.637	.076	0.927	9.90	.529
19	10.1	6.396	2.5	555	1016	"	6.934	.031	.734	.100	1.184	....	....
20	10.2	6.396	3	465	1016	"	6.131	.041	.606	.080	0.806	9.68	.557
21	10.2	6.396	3	400	1014	"	4.588	.034	.457	.042	0.467	....	....
22	10.3	6.396	3	500	1018	"	7.029	.059	.689	.099	1.080	11.86	.579
					Nitrogen of Urine = 45.939 Nitrogen of Fæces = 1.822 Nitrogen of Hair = 1.265								
Totals . . .		51.200	17	3777			49.026	0.310	4.762	0.569	6.754	34.17	1.822
Daily Averages		6.400	2.1	472			6.128	0.039	0.595	0.071	0.844		0.228

THIRD EXPERIMENT.—SECOND AFTER PERIOD.

Date.	Body.	Food.	Urine.								Feces.	
1897.	Weight.	Nitrogen.	Vol.	Sp. gr.	Reaction.	Nitrogen.	Uric Acid.	Total SO_3.	Combined SO_3.	Total P_2O_5.	Dry Weight.	Nitrogen.
May.	kilos	grams	c.c.		litmus	grams						
23	10.3	6.396	402	1015	Acid.	5.424	0.051	0.597	0.075	0.671	3.95	0.192
24	10.3	6.396	445	1010	Alkaline.	3.957	.028	.394	.031	0.289	....	....
25	10.1	6.410	620	1014	Acid.	7.224	.066	.787	.077	1.115	....	....
26	10.2	6.410	521	1013	"	5.730	.051	.541	.045	0.911	9.76	.542
27	10.1	6.410	550	1014	"	5.614	.039	.601	.050	0.892	....	....
28	10.1	6.410	470	1016	"	6.518	.033	.722	.066	1.103	....	....
29	10.2	6.410	455	1013	Alkaline.	4.994	.041	.549	.043	0.692	....	....
30	10.3	6.410	480	1017	Acid.	6.977	.045	.769	.065	1.113	15.04	.731
				Nitrogen of Urine = 46.438								
				Nitrogen of Fæces = 1.465								
				Nitrogen of Hair = 1.227								
Totals . . .		51.252	3943			49.130	0.354	4.960	0.452	6.786	28.75	1.465
Daily Averages		6.406	493			6.141	0.044	0.620	0.056	0.848		0.183

THIRD EXPERIMENT. — SECOND BORAX PERIOD.

Date.	Body.	Food.	Borax.	Urine.								Fæces.	
1897. May.	Weight.	Nitrogen.		Vol.	Sp. gr.	Reaction.	Nitrogen.	Uric Acid.	Total SO_3.	Combined SO_3.	Total P_2O_5.	Dry Weight.	Nitrogen
	kilos	grams		c.c.		litmus	grams						
31	10.1	6.410	10	530	1027	Alkaline.	7.711	0.053	0.836	0.070	1.474	....	....
June 1	10.1	6.410	10	420	1029	"	6.384	.037	.671	.052	1.102	....	....
2	10.3	6.410	5	360	1026	"	6.627	.029	.761	.099	0.998	19.10	0.874
3	10.4	6.410	6	342	1020	"	4.574	.029	.495	.038	0.336	....	....
4	10.3	6.392	7	540	1022	"	8.025	.042	.828	.113	1.112	....	....
5	10.2	6.374	10	450	1025	"	5.634	.031	.610	.077	0.680	19.40	1.019
6	10.2	6.374	8	502	1023	"	6.495	.040	.629	.070	1.005	....	....
7	10.3	6.374	8	513	1023	"	6.913	.034	.683	.076	0.809	17.55	0.844
					Nitrogen of Urine = 52.363 Nitrogen of Fæces = 2.737 Nitrogen of Hair = 0.932								
Totals . . .		51.154	64	3657			56.032	0.295	5.513	0.595	7.516	56.05	2.737
Daily Averages		6.394	8	457			7.004	0.037	0.689	0.074	0.939		0.342

THIRD EXPERIMENT.—THIRD AFTER PERIOD.

Date.	Body.	Food.	Urine.								Fæces.	
1897.	Weight.	Nitrogen.	Vol.	Sp. gr.	Reaction.	Nitrogen.	Uric Acid.	Total SO_3.	Combined SO_3.	Total P_2O_5.	Dry Weight.	Nitrogen.
June.	kilos	grams	c.c.		litmus	grams						
8	10.3	6.374	411	1016	Acid.	6.213	0.042	0.567	0.033	0.644	....	....
9	10.3	6.374	525	1013	"	5.834	.029	.558	.043	0.686	....	....
10	10.4	6.374	422	1011	"	4.284	.042	.447	.047	0.399	....	....
11	10.4	6.374	500	1014	"	6.149	.037	.638	.058	0.872	....	....
12	10.4	6.374	525	1016	"	7.560	.051	.781	.075	1.344	22.80	0.895
13	10.3	6.409	503	1013	Alkaline.	5.158	.043	.518	.030	0.644	....	....
14	10.2	6.445	652	1015	Acid.	7.917	.040	.856	.082	1.445	....	....
15	10.2	6.445	512	1012	"	5.663	.044	.631	.065	0.793	20.06	1.194
				Nitrogen of Urine = 48.778 Nitrogen of Fæces = 2.089 Nitrogen of Hair = 0.963								
Totals . . .		51.169	4050			51.830	0.328	4.996	0.433	6.827	42.86	2.089
Daily Averages		6.396	506			6.479	0.041	0.624	0.054	0.853		0.261

THIRD EXPERIMENT.—GENERAL SUMMARY.

Periods.	Total Nitrogen.			Urine.						Feces.		Hair.
	Ingested.	Excreted.	Balance.	Vol.	Nitrogen.	Uric Acid.	Total SO_3.	Combined SO_3.	Total P_2O_5.	Dry Weight.	Nitrogen.	Nitrogen.
	grams			c.c	grams							
Normal . .	52.163	51.734	+0.429	4196	49.093	0.315	4.515	0.495	7.738	24.69	1.417	1.224
Borax . . .	50.885	51.686	−0.801	3761	48.324	.293	4.905	.662	7.374	43.75	2.176	1.186
After . . .	50.995	50.334	+0.661	3962	47.430	.248	4.856	.562	7.519	39.66	1.845	1.059
Boric Acid .	51.200	49.026	+2.174	3777	45.939	.310	4.762	.569	6.754	34.17	1.822	1.265
After . . .	51.252	49.130	+2.122	3943	46.438	.354	4.960	.452	6.786	28.75	1.465	1.227
Borax . . .	**51.154**	**56.032**	**−4.878**	**3657**	**52.363**	**.295**	**5.513**	**.595**	**7.516**	**56.05**	**2.737**	0.932
After . . .	51.169	51.830	−0.661	4050	48.778	.328	4.996	.433	6.827	42.86	2.089	0.963

Throughout the entire experiment of fifty-six days the animal remained perfectly well, kept a fairly constant body-weight, and showed no symptoms of nausea or vomiting during the administration of either borax or boric acid. The only noticeable effect was a seeming loss of appetite on one day, as mentioned above. At the termination of the final after period, a single dose of 5 grams of boric acid was given. This resulted in vomiting 4–5 hours afterward.

The relative excretion of nitrogen for the seven periods is shown in the following table:

	1. *Fore Period.*		2. *First Borax Period.*		3. *First After Period.*	
Nitrogen of Food		52.163		50.885		50.995
Nitrogen of Urine	49.093		48.324		47.430	
Nitrogen of Fæces	1.417	51.734	2.176	51.686	1.845	50.334
Nitrogen of Hair	1.224		1.186		1.059	
Nitrogen Balance		+ 0.429		— 0.801		+ 0.661
Ratio of Urine and Hair Nitrogen to Food Nitrogen	96.4 per cent.		97.2 per cent.		95.0 per cent.	

	4. *Boric Acid Period.*		5. *Second After Period.*		6. *Second Borax Period.*	
Nitrogen of Food		51.200		51.252		51.154
Nitrogen of Urine	45.939		46.438		52.363	
Nitrogen of Fæces	1.822	49.026	1.465	49.130	2.737	56.032
Nitrogen of Hair	1.265		1.227		0.932	
Nitrogen Balance		+ 2.174		+ 2.122		— 4.878
Ratio of Urine and Hair Nitrogen to Food Nitrogen	92.2 per cent.		93.0 per cent.		104.1 per cent.	

	7. *Third After Period.*	
Nitrogen of Food		51.169
Nitrogen of Urine	48.778	
Nitrogen of Fæces	2.089	51.830
Nitrogen of Hair	0.963	
Nitrogen Balance		— 0.661
Ratio of Urine and Hair Nitrogen to Food Nitrogen	97.2 per cent.	

In the first borax period of eight days with a total consumption of 32.5 grams of borax, *i. e.*, an average of 4 grams per day, there is practically no change in the rate of proteid metabolism. There is, however, a slight rise in the amount of fæcal nitrogen similar to that noticed in the first experiment with borax, by which the nitrogen

balance is somewhat changed, but there is plainly no effect produced on proteid metabolism. In the second borax period, on the other hand, there is evidence for the first time of a distinct and unquestionable influence upon proteid metabolism. In this period of eight days 64 grams of borax were administered, and under its influence the excretion of nitrogen through the urine was greatly increased. As in the other experiments, the proportion of nitrogen in the fæces was likewise increased, implying decreased assimilation of proteid food, but the nitrogen balance of -4.878 is mainly due to direct stimulation of proteid metabolism. When, however, it is considered that to accomplish this result a daily dose of 8 grams of borax was required, and for eight consecutive days, with a dog weighing only 10 kilos, it is very plain that proteid metabolism is not readily affected by borax.

In the boric acid period of eight days, with a total dosage of 17 grams of the acid, there is some evidence of diminished proteid metabolism. The excretion of nitrogen through the urine is certainly diminished; there appears to be a sparing of proteid, but it is to be noticed that, in the period following, the nitrogen balance remains unaltered, which fact casts some doubt upon the assumption that the result is due solely to the acid. It is of course possible that the action of the boric acid may be continued into the after period, but this we should hardly expect in view of the rapid elimination of boric acid from the system. Further, after the second borax period, where the nitrogen balance is so noticeably disturbed, there is a quick return to the normal, the nitrogen balance for the final period dropping back to -0.661. Consequently, while the analytical data show a retention of nitrogen during the boric acid period, thus indicating diminished proteid metabolism, we feel some hesitation in attributing the result wholly to the boric acid, particularly as the earlier experiment with boric acid gave essentially negative results.

Especially noticeable in this experiment, as in the earlier experiment with borax, is the action of the latter agent in reducing the volume of the urine. [See table showing general summary.] In both borax periods the total volume of urine excreted is distinctly reduced, and the same holds true in this experiment with the boric acid. It is quite probable that the somewhat larger daily dose of boric acid made use of in the present experiment is responsible for this result, although it is possible of course that the personality of the animal may have had some influence. In the previous experiment

with boric acid, where the maximum daily dose was 2 grams, the volume of the urine was unaltered. In view of these facts it is perhaps proper to consider the larger dosage of boric acid used in the present experiment as responsible for the apparent action upon proteid metabolism likewise.

Also noticeable in this experiment is the influence of the larger doses of borax upon the excretion of total and combined sulphuric acid. Both of these are distinctly increased in amount during the last borax period, in harmony with the increase in proteid metabolism, and there is a suggestion of the same influence in the first borax period. Moreover, in the last borax period the excretion of phosphoric acid is noticeably increased, while the elimination of uric acid is slightly diminished. It is thus plainly evident, as already stated, that while moderate doses of borax, even long-continued, are without influence upon the nutritional processes of the body, large doses may distinctly increase the rate of proteid metabolism, giving rise not only to an increased excretion of nitrogen, but also of sulphuric acid and phosphoric acid.

In all of these experiments with borax there is constant evidence of an increase in the weight of the fæces during the borax periods. This increase in weight is due in part to an increased output of nitrogenous matter through this channel, but whether the latter is caused by diminished digestion and absorption of the proteid food or to a stimulation of the mucous or other secretions from the gastro-intestinal tract is not so clear. It has been plainly shown, however, in another connection[1] that while borax in moderate quantities has no inhibitory action whatever on either gastric or pancreatic digestion of proteids, larger proportions do retard the proteolytic action of both digestive fluids. Further, retardation of proteolysis with borax is much more pronounced than with boric acid; hence it seems quite probable that the increased bulk of fæces and the higher content of nitrogen therein during the borax periods is due mainly to slight retardation in the assimilation of proteid food.

Large amounts of borax likewise interfere with the assimilation of fatty foods; a statement which does not appear to be true of boric acid. In the accompanying table [page 37] are given the results of our analyses of the dry fæces, from a study of which it is plain that under the influence of large doses of borax — first and second borax

[1] Chittenden: Influence of Borax and Boric Acid on Digestion. Dietetic and Hygienic Gazette, 1893, vol. 9, p. 25.

periods of experiment third — both the total and percentage amounts of ether-soluble matter in the fæces are greatly increased. Boric acid, on the other hand, produces no such effect. In the first experiment, with borax, the evidence of decreased fat absorption is less pronounced, although both the dosage of borax and the amount of fat fed were greater than in the first borax period of experiment third. Quite possibly this apparent difference in action may be due to the personality of the animal. However this may be, it is plain that large doses of borax are prone to increase somewhat the bulk of the fæces, in part by diminishing slightly the assimilation of both proteid and fatty food, and in part, we think, through a tendency to increase the secretion of mucus. Thus, we observed in the last experiment, during the period when the largest doses of borax were given, that the fæces were more slimy than in the normal periods, and appeared to contain more mucus than ordinarily. Further, it is to be noted that under the influence of large doses of borax there is a tendency toward diarrhœa; not very marked to be sure, but sufficient to render the discharge of fæces somewhat watery.

In spite of these evidences of minor action in the intestinal tract with large doses of borax, there is no evidence whatever of any influence exerted upon intestinal putrefaction, either by borax or boric acid. Even with the largest doses of borax the combined sulphuric acid of the urine is raised rather than lowered, and careful examination of the urine daily with Jaffe's indoxyl test failed to reveal any indications pointing to an inhibitory influence exerted by either borax or boric acid upon the production of indican. If, however, one studies carefully the output of combined sulphuric acid as shown in the various tables it will be noticed that the highest figures are generally obtained on the day (or the day preceding that) on which the dog defecates; while after defecation the combined sulphuric acid of the urine falls at once. In other words, the natural obstruction of the intestine favors, as is well known, the absorption of putrefactive products, and thus leads to an increase of combined sulphuric acid in the urine. When, on the other hand, defecation occurs, the combined sulphuric acid of the urine is at once diminished in amount. Upon these natural fluctuations of combined sulphuric acid even the largest doses of borax and boric acid are without effect, not because these agents are without influence upon micro-organisms, but because they are too rapidly and completely absorbed from the intestine to exert much influence upon intestinal putrefaction. In only one in-

TABLE SHOWING CONTENT OF FAT AND OTHER ETHER-SOLUBLE MATTER IN THE FÆCES.

EXPERIMENT I.

Date.	*Fæces.*	*Ether-soluble matter.*		*Period.*
1896.	Dry weight. Grams.	Per cent.	Grams.	
Dec. 2	38.15	35.03	13.362	Fore
7	35.91	33.60	12.067	
11	24.68	25.23	6.227	
	60.59	30.02	18.294	Borax
16	33.25	36.51	12.140	
20	25.45	24.36	6.198	
	58.70	31.24	18.338	After

EXPERIMENT II.

Date.	*Fæces.*	*Ether-soluble matter.*		*Period.*
1897.	Dry weight. Grams.	Per cent.	Grams.	
Feb. 26	6.96	23.70	1.649	
Mar. 2	11.90	17.88	2.128	
3	10.50	16.95	1.770	
5	17.30	20.82	3.602	
	46.66	19.61	9.149	Fore
8	10.20	18.87	1.924	
10	9.75	17.67	1.723	
12	16.30	20.31	3.311	
14	11.60	20.60	2.390	
15	5.45	20.54	1.119	
	53.20	19.67	10.467	Boric Acid
16	5.45	20.54	1.119	
17	7.71	26.63	2.053	
19	8.82	20.28	1.789	
21	12.25	20.72	2.538	
23	10.47	20.01	2.095	
25	10.90	19.31	2.105	
	55.60	21.04	11.699	After

EXPERIMENT III.

Date.	*Fæces.*	*Ether-Soluble matter.*		*Period.*
1897.	Dry weight. Grams.	Per cent.	Grams.	
Apr. 25	14.33	28.91	4.134	
28	10.36	29.09	3.029	
	24.69	29.01	7.163	Normal
29	2.96	29.09	0.840	
May 3	20.10	36.35	7.306	
6	20.69	37.06	7.671	
	43.75	36.15	15.817	Borax
11	19.55	36.18	7.091	
13	11.90	23.50	2.797	
14	8.21	25.89	2.117	
	39.66	30.27	12.005	After
15	2.73	25.89	0.705	
18	9.90	33.19	3.286	
20	9.68	25.76	2.499	
22	11.86	24.13	2.858	
	34.17	27.36	9.348	Boric Acid
23	3.95	24.13	0.953	
26	9.76	24.20	2.372	
30	15.04	29.54	4.443	
	28.75	27.02	7.768	After
June 2	19.10	45.01	8.596	
5	19.40	39.06	7.579	
7	17.55	33.94	5.940	
	56.05	39.46	22.115	Borax
12	22.80	39.27	8.954	
15	20.06	29.99	6.028	
	42.86	34.96	14.982	After

stance were we able to detect any boric acid in the faeces, viz., on June 5th, at a time when the largest doses of borax were being given; and at the close of this period the boric acid reaction could be obtained with the urine only on the first day of the after period, so rapidly was the borax passed out of the body.

Lastly, attention may be called to the constant presence, in appreciable amounts, of uric acid in the urine of all the animals experimented with, in opposition to the older statements of Liebig[1] and others that kynurenic acid may entirely replace uric acid in the urine of the dog. Our results, so far as they extend, are thus wholly in accord with the recent observations of Solomin.[2] We have, however, made no attempt to determine the amounts of kynurenic acid present.

General Conclusions.— Moderate doses of borax up to 5 grams per day, even when continued for some time, are without influence upon proteid metabolism. Neither do they exert any specific influence upon the general nutritional changes of the body. Under no circumstances, so far as we have been able to ascertain, does borax tend to increase body-weight or to protect the proteid matter of the tissues.

Large doses of borax, 5–10 grams daily, have a direct, stimulating effect upon proteid metabolism, as claimed by Gruber; such doses, especially if continued, lead to an increased excretion of nitrogen through the urine, also of sulphuric acid and phosphoric acid.

Boric acid, on the other hand, in doses up to 3 grams per day, is practically without influence upon proteid metabolism and upon the general nutrition of the body.

Borax, when taken in large doses, tends to retard somewhat the assimilation of proteid and fatty foods, increasing noticeably the weight of the faeces and their content of nitrogen and fat. With very large doses there is a tendency toward diarrhœa and an increased excretion of mucus. Boric acid, on the contrary, in doses up to 3 grams per day, is wholly without influence in these directions.

Borax causes a decrease in the volume of the urine, changes the reaction of the fluid to alkaline, and raises the specific gravity, owing to the rapid elimination of the borax through this channel. Under no circumstances have we observed any diuretic action with either borax or boric acid. The latter agent has little effect on the volume of the urine.

[1] Liebig: Annalen d. Chem. u. Pharm., Band 86, p 125.

[2] Solomin: Zur Kenntniss der Kynurensäure. Zeitschr. f. physiol. Chem., 1897, Band 23, p. 497.

Both borax and boric acid are quickly eliminated from the body through the urine, twenty-four to thirty-six hours being generally sufficient for their complete removal. Rarely are they found in the faeces.

Neither borax nor boric acid have any influence upon the putrefactive processes of the intestine as measured by the amount of combined sulphuric acid in the urine, or by Jaffe's indoxyl test. Exceedingly large doses of borax are inactive in this direction, not because the salt is without action upon micro-organisms, but because of its rapid absorption from the intestinal tract.

Borax and boric acid, when given in quantities equal to 1.5–2.0 per cent of the daily food are liable to produce nausea and vomiting.

Owing to the rapid elimination of both borax and boric acid, no marked cumulative action can result from their daily ingestion in moderate quantities.

At no time in these experiments was there any indication of abnormality in the urine; albumin and sugar were never present.

VARIATIONS IN DAILY ACTIVITY PRODUCED BY ALCOHOL AND BY CHANGES IN BAROMETRIC PRESSURE AND DIET, WITH A DESCRIPTION OF RECORDING METHODS.*

By COLIN C. STEWART, A. B., Toronto.
Fellow in Physiology, Clark University.

[*From the Laboratory of Physiology, Clark University, Worcester, Mass., U.S.A.*]

IN a series of papers dealing with the laws of growth Minot[1] has pointed out the significance of experiments on organisms as individual wholes, as leading toward the proper object and final purpose of biological investigation, — the discovery of the laws of life. Growth, anabolic and accumulating, has its reverse in all forms of katabolism, of which by far the most important are the forms which supply from day to day and from hour to hour energy for those bodily functions which may be summed up under the broad name of "activity." If we grant that the activity of any individual organism may be an index of the sum total of its bodily conditions, then the study of the variations of that activity, and of the conditions which lead to such variations, becomes of the utmost importance.

With the commencement of such a study its difficulties begin. How is it possible to arrive at an adequate estimate of such activity? The present methods of Science can measure metabolism but exact chemical analyses would be impossible in a long series of experiments on normal animals. It becomes then clearly necessary to make many assumptions in devising a practicable method. In the research about to be described it has been assumed that the amount of muscular energy developed, in other words the amount of work

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COLIN C. STEWART.

done, by any animal day by day will be an approximate expression of its susceptibility to those variable conditions which may be chosen for experimentation. But here again new obstacles arise. No animal, even under conditions which may seem to be unvaried, will spontaneously show a uniform degree of activity for any series of days. Small causes, apparently inappreciable and unmeasurable, will produce changes tending to create or to destroy that feeling of bodily well-being which accompanies the proper functioning of all component parts. In studying the effect of drugs, for example, this difficulty becomes so overwhelming that it is plain that these small causes must be investigated for themselves. Weather changes, long recognized as potent, must be studied. The effects of atmospheric pressure, atmospheric moisture, temperature, light, winds and electrical variations must be obtained by long series of observations before we can hope to arrive at a solution of our single equation with its almost indefinite number of unknown quantities.

Of the meteorological factors just mentioned, only atmospheric pressure has been taken into consideration here. The methods of the research have nevertheless been applied for the purpose of studying the effects upon activity of variations in diet, and of the administration of alcohol, with the hope of obtaining results so broad and general as to be of value in showing at least the possibilities in this comparatively new field of operation.

So much for the purpose and aims of the undertaking. A word must be said as to the selection of suitable animals for the experiments. It seemed best to choose rats and mice, because they fill as many as possible of the requirements. They are small, cheap, easily fed and cared for; and, best of all, when placed in revolving cages they spend most of their time, when not eating or sleeping, in running.

With regard to the distribution of their working periods it may be noted that the records obtained from rats show that their activity is confined entirely to the hours of the night. Beginning at from six to eight o'clock in the evening — later in summer than in winter — they are uniformly, though not continuously, active during the next eight or ten hours. Contrasted with this is the activity of the squirrel, the records of which show greater intensity, but only for an hour or two night and morning. Still another type was that of two fox-squirrels, active throughout the whole of the day and sleeping only at night. Such differences indicate that an investigation of the

comparative distribution of activity and of the relation of its intensity to its duration promises interesting and valuable results. [1] Commencing, as did Hodge and Aikins,[2] with the protozoa, it might be possible to develop much that would bear closely upon theories of animal rhythm, rest and sleep.

The following section will give a detailed account of the apparatus used, and of the general methods of procedure.

Description of Apparatus and Methods. — The apparatus consists primarily of two parts : the cages in which the animals to be experimented upon are placed, and the various mechanisms for recording their movements in these cages. Each of the cages (see Fig. 1) used throughout the experiments on rats is cylindrical, eighteen inches long by twenty in diameter, made of fine wire netting soldered to a

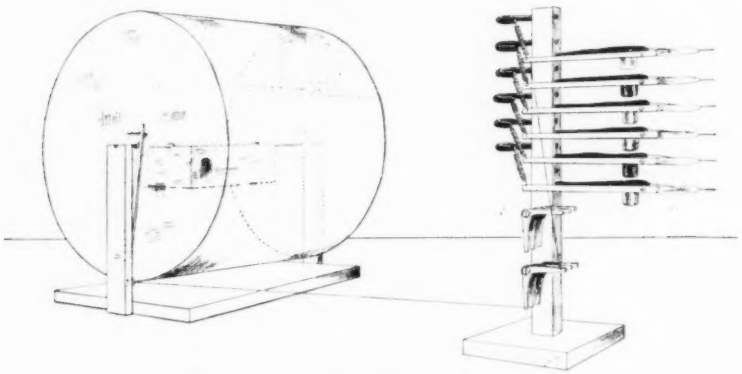

FIGURE 1.

frame of stout steel wire. The cage revolves freely on a steel rod supported by a fixed wooden frame. At one end is a wide-hinged door; from the axle is hung a light wooden nest-box, completely closed in but for a small round opening on one side; and to the end of the nest-box next the door is fixed a detachable tin feed-box of two compartments. At the opposite outer end of the cage is an eccentric which, with each revolution of the cage in either direction, pushes aside an upright lever attached to the wooden axle support, and in so doing pulls the wire connecting the cage lever with the recording apparatus.

Cages used for mice are similar in construction, except that their small size (eight inches long by five in diameter) renders them so

light that no wooden support is needed for the axle. The axle is held in position by a clamp upon an iron standard, while a second clamp holds a bearing for the lever which, with its wire, serves as a means of communicating the motions made by the cage.

To record the revolutions of the cages a simple six-inch continuous-roll kymograph, with uniform motive power, was first used. A standard carrying six light wooden levers, each five inches long, is placed before the kymograph. Each lever is tipped with thin whalebone, and to each is fixed a small glass ink-well and a pen of fine capillary glass tubing. Each is connected by a wire to the lever of the corresponding animal cage. As the cage revolves the eccentric pushes back the cage lever, the wire attached to it is pulled, the pen lever is drawn down, and the pen makes a vertical mark upon the slowly travelling scroll of paper. Upon the release of the cage lever a spring fastened to the pen draws the pen, the wires and the cage lever back to their original position, and the apparatus is ready to record another revolution of the cage.

Single revolutions would be indicated by single vertical lines, but when the cage is made to revolve with sufficient rapidity a continuous broad band marks the duration of a series of revolutions. An electro-magnetic time-marker, connected with a battery and a clock making short connections every minute and longer ones every hour, gives an accompanying record by means of which the duration and distribution of such periods of activity may be computed.

The kymograph method just described, though invaluable in the study of the distribution of activity throughout the day in different species of animals, and even in different animals of the same species, is nevertheless a rather unreliable one for close or accurate experimental measurement. After a rate of cage revolution has been reached which is sufficiently great to be recorded by a continuous broad band, no greater speed of revolution can be distinguished by any feature of the tracing. In other words, of two animals one might do twice as much work as the other in the same period of time without any indication of that fact being shown upon the record of their activity.

A much more exact recording method is the following, which has been used in almost all the experiments to be described. The hair spring and balance wheel of a common spring clock are removed, and to the escapement are attached, on one side a soft spring of fine brass wire, and upon the other a wire which, passing through a slit-

like opening in the clock case, is in turn attached, as was the wire in the preceding method, to the cage lever. Each revolution of the cage, as before, pulls the wire, the escapement is drawn down, and one cog of the ratchet wheel is let go. In the clocks used two of these cogs correspond to one second on the dial — seven thousand two hundred, therefore, to an hour. The clock is set at twelve, and the exact number of revolutions performed in any given time by the cage to which it is attached may, at the end of that time, be read off on the dial. This method fails to give any representation of the distribution of activity, but its relative accuracy in recording the total amount of work done makes it perhaps the most useful in experiments where daily variations due to food and drug effects are being sought for. By estimating the circumference of the cage used, and multiplying by the observed number of revolutions in any given time, one may obtain a rough estimate of the distance travelled. For example, it was noted in the course of the various experiments to be described, that a common gray rat will run normally from five to fifteen miles in a single night, one particularly active rat travelling an aggregate distance of one hundred and forty-three miles in ten days.

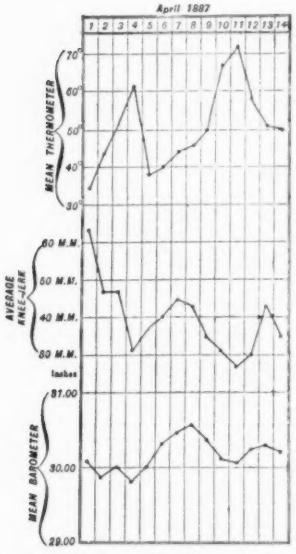

FIGURE 2. Knee-jerk, barometer and thermometer. (Lombard)

In a third piece of recording apparatus, not so well adapted for prolonged experiments, but possessing in a measure the advantages of the preceding two, instead of turning the hands on the dial, as in the second method, a similar clock is made to wind up a cord which runs on a bobbin fastened to the axle of the hour hand. The cord is attached to a vertically moving stylographic pen which records its position on a slowly travelling roll of paper. When the cage is not revolving the pen is at rest and traces a horizontal line; but when it is revolving, the pen slowly rises as the string is wound up. By using a roll of paper carried on a kymograph at the rate of six or eight inches a day, and recording also thermometer, barometer, hygrometer and

time, a more or less complete picture of the data for the period studied may be obtained.

The Effect upon Activity of Changes in Barometric Pressure. — Lombard[3] has described a correspondence between the variations of average knee-jerk for a series of days, and the condition of the weather. His results (see Fig. 2) show a direct relation between knee-jerk and barometric pressure, and a more indefinite inverse relation to temperature. No effect of changes in humidity, or in electric tension, was shown. Lombard[4] has also shown, in experiments upon himself, that a decrease in atmospheric pressure lessens the ability to do voluntary muscular work, while an increase in pressure increases muscular power. High temperature, especially when associated with much humidity, decreases this ability.

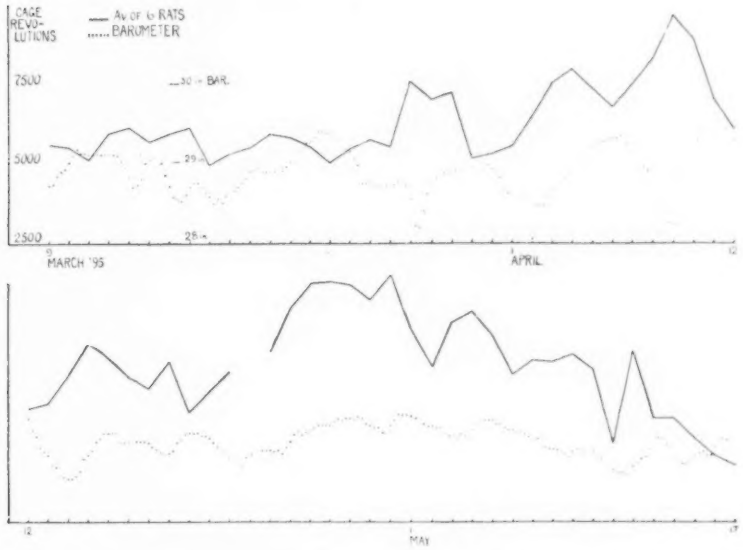

FIGURE 3. Curve of the average daily activity of six gray rats, during seventy days. The dotted line shows barometric pressure.

An undoubted influence of barometric variations upon the activity of the nerve muscle complex has, therefore, already been demonstrated, so that we might naturally expect to find variations in the amount of spontaneous daily work correlated with changes in atmospheric pressure. Turning to the experiments in which the methods

already outlined were used, we have in Figure 3 a curve, plotted in terms of cage revolutions, for seventy days, of the average daily activity of six common gray rats, full grown when caught, and therefore uninfluenced by domestication. The dotted line shows the variations in barometric pressure during the continuance of the experiment. Up to April twelfth, that is during the first half of the time, the rats were perfectly normal. During the latter half, however, four of them were getting alcohol in addition to their regular food. The consequent interference with normal activity is shown in the otherwise unaccountable rise during the latter part of April and the first few days of May. This will be referred to again more fully when the alcohol experiments are being described.

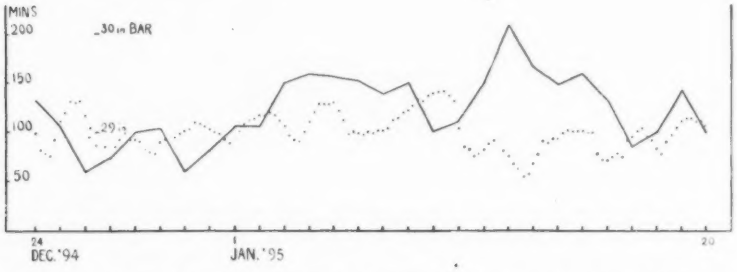

FIGURE 4. Curve of the daily activity in minutes of a single gray rat during twenty-six days. Barometer, as before, in dotted line.

Figure 4 is a curve of the variations in duration of activity shown by a single gray rat during twenty-six days. The curve of barometric pressure is superimposed in dotted line. In each of these curves there is shown an inverse relation between the amount of daily activity and the barometric pressure. Similar results were obtained from the records of a common red squirrel, though the squirrel's activity showed at times extreme variations from day to day with no apparent cause.

Figure 5 shows curves of the variations in daily activity of three groups of white rats for one hundred and twelve days. For the first twenty-six days the record is from five pairs of rats, one pair, male and female, to a cage; for the next twenty-six days six pairs are recorded, five of them being the five pairs of the preceding days; and for the rest of the time a new series of six pairs furnish the records. Where a point in the record has been enclosed in a

small circle, imperfect data have been used to fill out the space. The barometric pressure is recorded, as before, in dotted line.

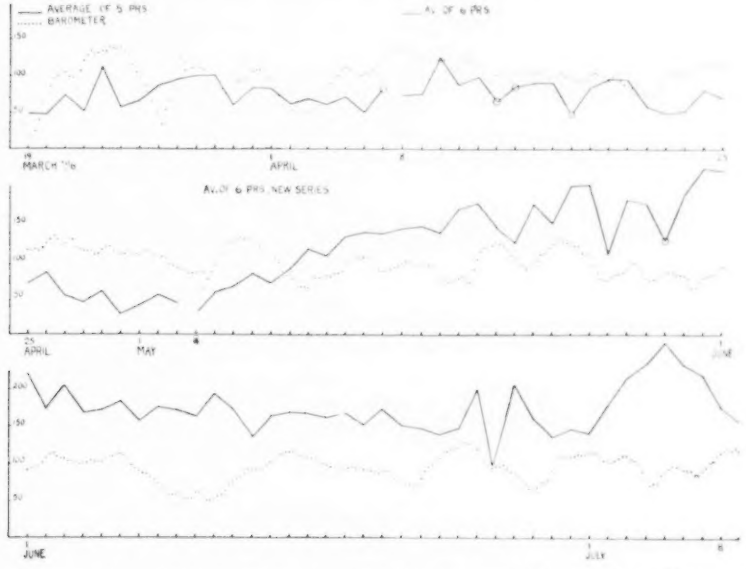

FIGURE 5. Curve of average daily activity of white rats: March 19th to April 7th, average of five pairs; April 8th to May 3d, of six pairs; May 4th to the end, of a new series of six pairs. Barometer in dotted line.

Whatever correspondence there is between the two curves would lead to the conclusion that the effect of changes in atmospheric pressure is a direct one, as against the inverse relation shown for gray rats. A point worthy of note, however, is that just as the pressure effect is shown more clearly in the curve of the first experiment where the animals are perfectly normal (see Fig. 3), so in this curve, from the beginning to the point marked April eighth, and from May fourth to June first, where the records are from normal rats, a correspondence is more clearly shown. During the rest of the time the same animals were being used for alcohol experiments, with a consequent interference as yet unexplained. Many of the daily variations in the curve are unaccounted for, but the great rise in average activity shown during the early part of July is without doubt due to the disturbing noises incident to the celebration of Independence Day.

Figure 6 gives another curve of the average activity of six white rats, with barometer plotted in dotted line as before. Here again the correspondence between the curves is only of doubtful value.

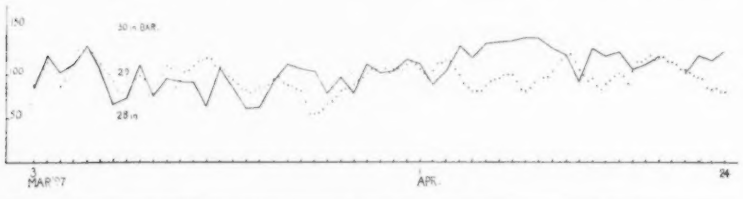

FIGURE 6. Average activity of six white rats for fifty-three days. Barometer in dotted line.

Figure 7 shows, in solid and broken line, the curves of activity of two dogs, from data obtained by Hodge[5] by means of a pair of ingeniously contrived pedometer watches carried by the dogs in their collars. The curves are plotted from the readings of these watches taken once a day. To the chart I have added in dotted line the curve of barometric pressure for the forty-six days of the experiment, with the result of establishing a somewhat striking correspondence. The curve would be improved in legibility if the records for the two dogs were averaged instead of being plotted

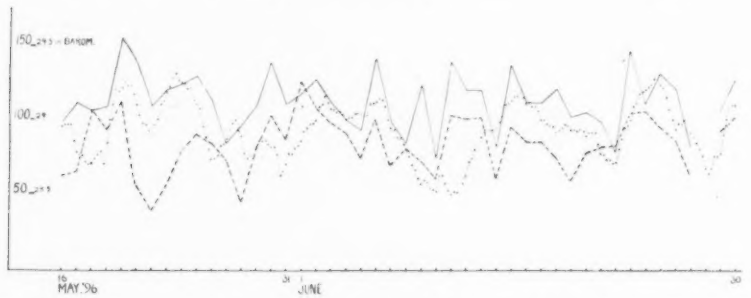

FIGURE 7. Curves of the activity of two dogs, plotted in solid and broken line. Barometric variations shown in dotted line for the forty-six days of the experiment.

separately, as they are in the figure; but it would not show, as it does now, the remarkable similarity between the two. Other measurable factors are undoubtedly at work in producing variations, — factors which can be determined only by manifold repetition of such experiments.

The foregoing charted results show an inverse relation between the amount of voluntary daily activity of gray rats and atmospheric pressure, and a direct relation between variations in barometric pressure and the activity of the two dogs. The white rats experimented upon showed only a doubtful direct relation between the amount of their daily activity and pressure. The experiments seem to point to the possibility of a fundamental difference in this respect between domesticated animals, independent of weather changes, and wild animals with their greater need of individual effort for self-preservation and their greater interest in food supply.

The Effect of Changes in Diet. — The experiments under this head were all upon white rats normally fed on a uniform diet of dog-biscuit and water. In the first experiment (see Fig. 8) six pairs of white rats, one pair to a cage, were used. The solid line shows the average daily activity of three pairs, the broken line that of the other three.

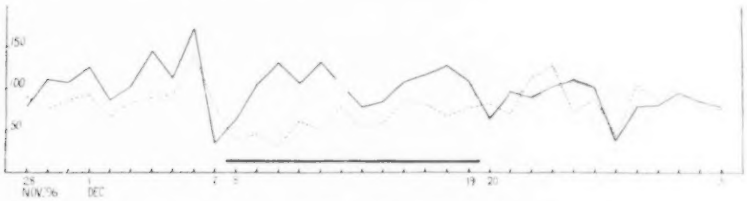

FIGURE 8. Feeding experiment. Each line shows a curve of the daily average of three pairs of white rats. From Dec. 8th to 19th those of the dotted line get beef and dog-biscuit, the others corn. For the rest of the time all were fed dog-biscuit.

Both groups were normal up to December seventh; then those represented by the broken line were fed fat and lean raw beef and dog-biscuit for twelve days, during which time the others got Indian corn. From the twentieth of December to the end of the experiment, twelve days again, all were fed dog-biscuit as before. The decrease in voluntary activity with the heavier diet is shown in the curve.

In the second experiment (see Fig. 9) all six pairs, the same rats as were used in the preceding experiment, were fed alike. For the first twelve days they were fed on dog-biscuit, with good average records as the result. During the next fifteen days (January first to fifteenth) white bread was given, with an accompanying increase in the amount of daily work. For the next ten days (January sixteenth to twenty-fifth) bread and fat and lean beef were given, causing a manifest decrease. Then for six days (January twenty-sixth to

thirty-first) bread alone, as before, was fed, with again a rise. This was followed by bread and beef for seven days (February first to seventh) with a fall in activity. From the eighth of February to the end of the experiment on the first of March bread alone was fed,

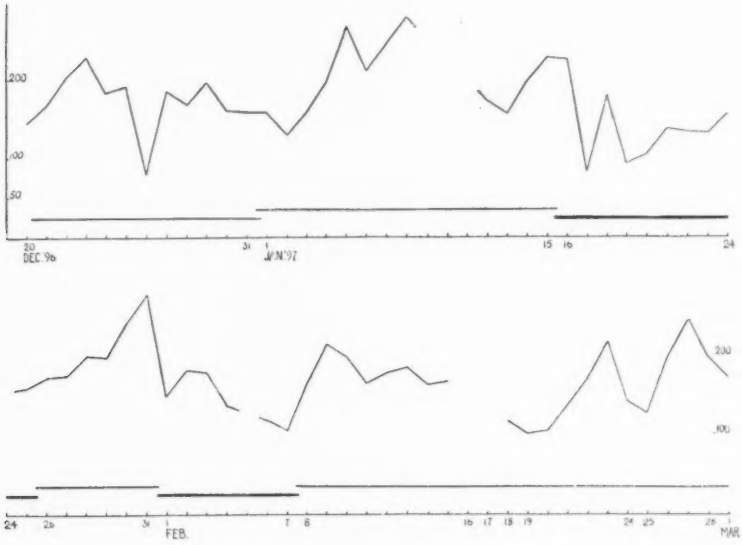

FIGURE 9. Second feeding experiment. Curve shows average activity of six pairs of white rats. December 20th to 31st — dog-biscuit. January 1st to 15th — bread. January 16th to 25th — beef and bread. January 26th to 31st — bread. February 1st to 7th — beef and bread. February 8th to March 1st — bread. At points marked February 18th and 19th the effect of lack of food is shown; at February 24th and 25th, the effect of an escape of gas, and the same at March 1st.

with a resulting rise in activity. The record for this last period remains uncomplicated, however, during only the first eight days. On the seventeenth of February the record for the preceding night was not noted, nor were the rats fed. The records for the sixteenth and seventeenth were therefore lost, while the records for the eighteenth and nineteenth show the effect of insufficient food. Recovery was complete by the twenty-third, when unfortunately gas escaped in the room in which the experiments were carried on, and several of the rats were noticeably poisoned by it — the effect upon their activity being shown by the records of the twenty-fourth and twenty-fifth. Re-

covery again followed, when, on the twenty-eighth, gas escaped once more, with a similar result.

The next figure shows in another way the result of this experiment (see Fig. 10). The average for each of the periods mentioned has been taken from the perfect records of that period, while the average activity for the whole time is also shown by a horizontal broken line.

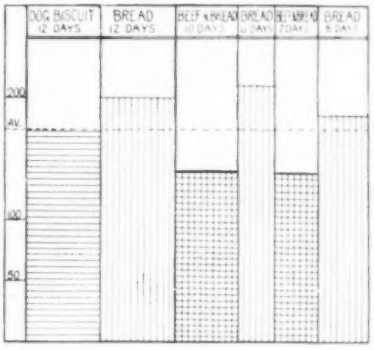

FIGURE 10. Another rendering of Figure 9, showing graphically the average activity for each of the periods of the second feeding experiment.

For the third feeding experiment (see Fig. 11) six male rats were selected, and all were fed on dog-biscuit for the first ten days. Then from the thirteenth to the thirtieth of March the three whose average activity is plotted by the broken line were fed beef, cheese, sugar, chocolate, and bread, while the other three, the solid line, got bread alone. From the thirty-first of March to the nineteenth of April the conditions were reversed, those previously well fed getting the meagre diet of bread. During the last five days the conditions were again reversed, with a

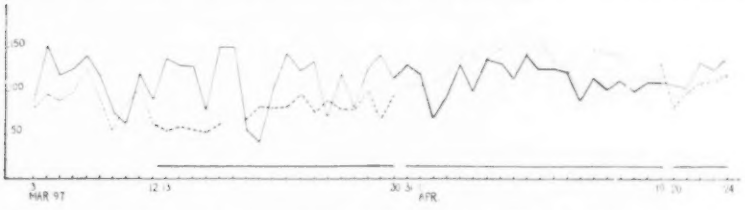

FIGURE 11. Third feeding experiment. Each line the average of the records of three male rats. All normal to March 12th. March 13th to 30th, full diet for those of the broken line and bread for the others. March 31st to April 19th, full diet for those of the solid line, and bread for the others. April 20 to 24th, the conditions again reversed.

second crossing of the lines of activity as the result. The simpler diet in all cases gives a relatively greater degree of activity. The weights of the rats were taken at the commencement of the experiment, at each change, and at the end. The following table shows the increase in weight that accompanied the decrease in activity.

Rat No.	March 3d. Commencement.	March 31st. After rich diet.	April 20th. After diet of bread.	April 25th. After rich diet.
1	305 g.	329 g.	310 g.	325 g.
2	312	335	322	325
3	235	249	238	240
	Commencement.	After diet of bread.	After rich diet.	After diet of bread.
4	315 g.	307 g.	332 g.	326 g.
5	300	281	286	280
6	260	231	256	255

Effect of Alcohol. — Hodge,[3] in the published account of his experiments on the physiological effect of alcohol on dogs, records the observation that the two alcohol dogs, although never intoxicated, show much less activity than the two normal controls. The use of a pair of pedometer watches developed the fact that, of the males, the alcoholic showed during forty-six days only seventy-one per cent of the activity of the other, while with the females the alcoholic showed a percentage of only fifty-seven.

In the first series of my own experiments gray rats were used. Six rats of as nearly equal weights as could be found were placed in six similar cages and kept on a normal and entirely uniform diet for longer or shorter periods before the actual commencement of the experiment. Averages of their activity for such periods were taken on April twelfth, 1895, and the rats were arranged in pairs in such a way that the total average activity of any one pair was as nearly equal to that of either of the other two pairs as possible. It was decided to give weak alcohol to two, strong alcohol to two, and to keep the other two as normal controls. Alcohol was administered with their food in increasing strength, according to the following schedule:

	April 12th.	15th.	22d.	27th.	May 2d.	6th.	10th.	14th.
Normals . .	0 %	0 %	0 %	0 %	0 %	0 %	0 %	0 %
Weak . . .	5	10	15	20	—	—	—	—
Strong . . .	5	10	15	20	30	40	50	60

So that one pair from April twenty-seventh to the end of the experiment in October of the same year drank nothing but twenty per cent alcohol, while another pair had a sixty per cent solution after May fourteenth.

Figure 12 shows the voluntary activity of these six rats during the experiment. The solid line is the curve of the average of the two normal rats, the dotted line that of the weak alcohol rats, and the

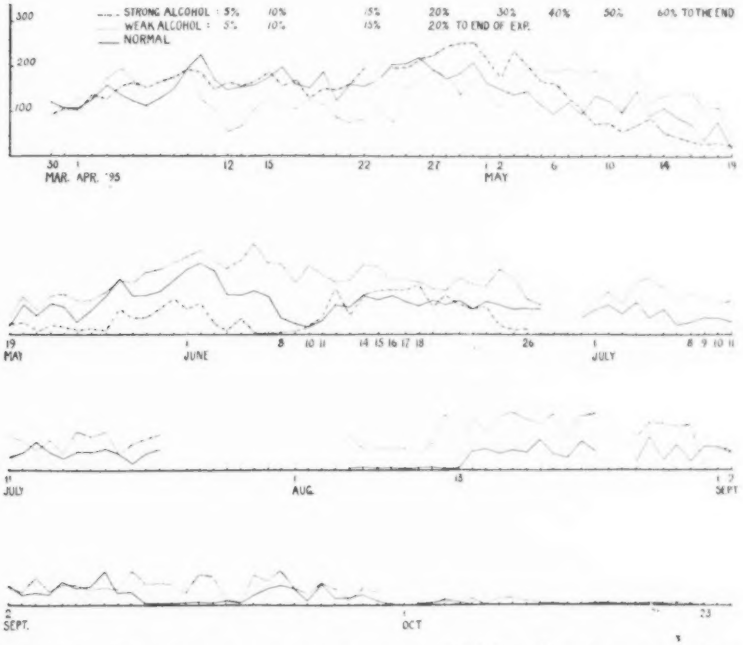

FIGURE 12. Alcohol experiment upon gray rats. Solid line plots the average of two normal rats; dotted line, of two getting weak alcohol; and broken line, of two getting strong alcohol. Water given June 8, 10, 11, 14, 15, 16, 17 and 18, and July 8, 9 and 10.

broken line, that of the strong. One of the rats getting the strong solution died on the seventeenth of May, the second on the twenty-sixth of June. On the eighth, tenth, eleventh, fourteenth, fifteenth, sixteenth, seventeenth and eighteenth of June, and on the eighth, ninth and tenth of July, water was substituted for alcohol. The result was a decided rise in the activity of the strong alcohol rats and no definite effect upon the weak alcohol animals. The

general falling off in activity toward the end of the experiment is no doubt partly due to the lack of variety and general insufficiency in diet.

Figure 13 gives another rendering of the same curve, with the normals plotted as a level line and the others shown as varying above and below that normal. The broken line is the curve of the strong

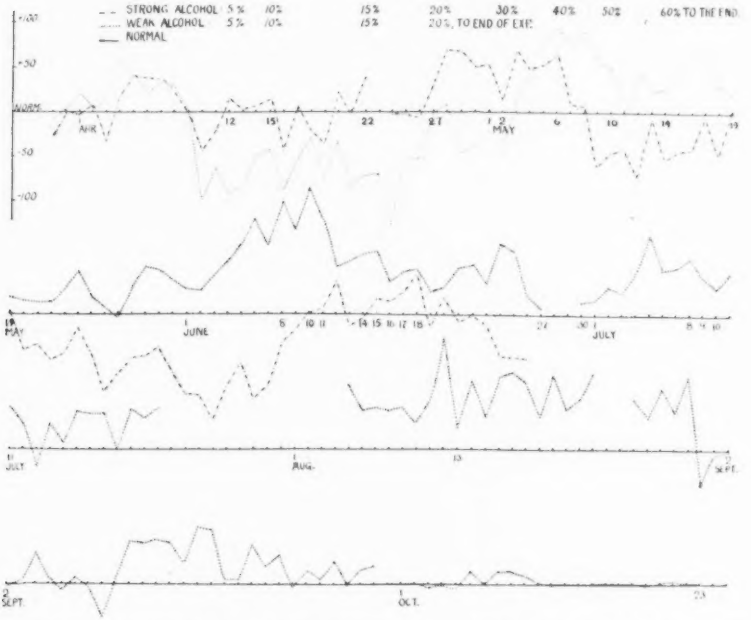

FIGURE 13. Another chart of the same experiment. Activity of normal rats taken as base line; strong alcohol rats in broken line, and weak alcohol rats in dotted line. Water given June 8, 10, 11, 14, 15, 16, 17 and 18, and July 8, 9 and 10.

alcohol rats, and the dotted line that of the weak. It shows perhaps better than Figure 12 the primary rise in the activity of the rats getting strong alcohol, with a subsequent fall as soon as forty per cent is given, and the rise again during the month of June when water was substituted. For the animals getting weak alcohol it shows a slower rise but no subsequent fall to the level of the normals for any length of time.

Figure 14 is a chart showing the result of an experiment upon six pairs of white rats, one pair, male and female, to a cage. Three

pairs are normal throughout, their average daily activity being plotted in solid line. The other three are normal for twenty-nine days, until June second, when five, ten, fifteen and twenty per cent alcohol are given on four successive days, the twenty per cent alcohol

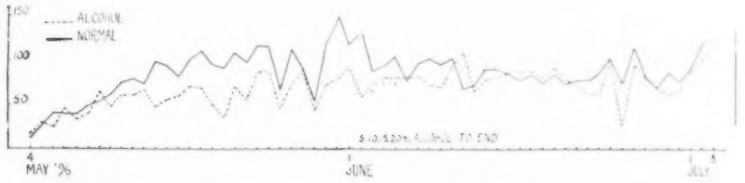

FIGURE 14. Alcohol experiment on white rats. Each line shows the average of three pairs — all normal until June first. Those shown in dotted line are then fed alcohol; the others, the solid line, are control animals.

being continued until the end of the experiment on July third. The curve shows no decrease as the result of administering alcohol in twenty per cent solution, but rather a relative increase. This curve, too, gives an example of increase through practice — a curve of getting used to the apparatus.

Figure 15 shows, for another experiment, a decrease in activity following immediately upon the administration of thirty per cent

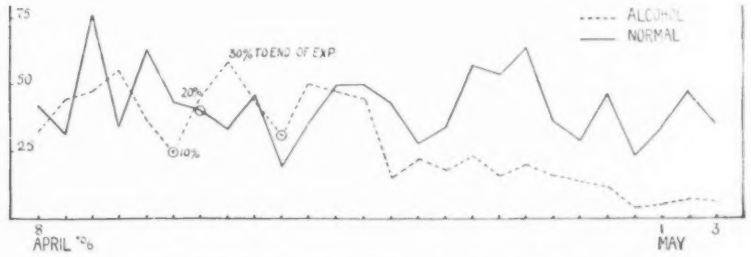

FIGURE 15. Alcohol experiment on white rats. Each curve shows the average of three pairs. The solid line shows the activity of the normal animals, the broken line that of the alcoholic animals. Alcohol given as indicated. Points enclosed in small circles are filled in from imperfect data.

alcohol. As in the preceding experiment, six pairs of white rats, three for alcohol and three for controls, were used. Points enclosed in circles are filled in from imperfect data.

Conclusions.

1. While the experiments show, for gray rats and for a red squirrel, an influence of barometric pressure on voluntary, spontaneous activity that indicates an inverse relation between the two, the curves for dogs, and possibly also for white rats, show a direct effect of atmospheric pressure in increasing voluntary activity. The difference may be due to a constant difference between domesticated and wild animals.

2. Influences other than barometric pressure are undoubtedly at work to produce variations which must be considered as normal.

3. The effect of a rich diet upon white rats is to decrease voluntary activity, while that of a plain though apparently sufficient diet is to increase it. This increase, in one experiment, has been correlated with a slight loss in weight, while the decrease was accompanied by a corresponding gain.

4. The activity of rats is markedly decreased by the administration of alcohol in thirty to sixty per cent solutions, but no decrease has been experimentally demonstrated as a result of giving a twenty per cent solution of pure alcohol.

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THE INFLUENCE OF HIGH ARTERIAL PRESSURES UPON THE BLOOD-FLOW THROUGH THE BRAIN.

By W. H. HOWELL.

[*Professor of Physiology, Johns Hopkins University.*]

THE conditions controlling the circulation of blood in the brain are peculiar, and offer an intricate physical problem the solution of which has been attempted from an experimental as well as from a purely theoretical standpoint. The fact that the brain is contained within a rigid box that does not permit free expansion of the organ, has led some authors to assume that dilatation of its arteries, however produced, is not followed by an increased flow of blood, as is usual in other organs, but on the contrary, under certain conditions at least, by a lessened flow. Thus, Geigel[1] has held upon theoretical grounds that dilatation of the arteries of the brain is accompanied by a compression of the capillaries, owing to the fact that the expansion of the arteries causes an increase in intracranial pressure that is transmitted to the capillaries. Upon this view, therefore, dilatation of the arteries, whether produced through vaso-dilator nerve fibres or by a rise in general arterial pressure, should be followed by a lessened flow of blood through the brain, and *vice versa*.

Grashey[2] in his well-known treatise upon the hydro-statics and hydro-dynamics of the cerebral circulation has also admitted a similar possibility. Grashey assumes that intracranial pressure depends upon two conditions, namely, the volume of the cerebro-spinal liquid and the amount of arterial pressure. Dilatation of the arteries must lead to an increased intracranial pressure, and this being transmitted through the brain substance acts upon the part of the circulation where the intravascular pressure is least, that is, the cerebral veins. Inasmuch as the pressure within the capillaries is greater than in the veins, an increase of intracranial pressure should affect the veins and not the capillaries, as Geigel assumed. Moreover, Grashey emphasizes a fact that other authors seem sometimes to overlook, namely, that the sinuses of the brain are probably entirely protected from any direct influence of intracranial pressure by their tense and inextensible covering of dura mater. From his theoretical standpoint Grashey concludes that an increase in arterial pressure causes a greater flow

of blood through the brain up to a certain limit only. So soon as intracranial pressure is raised by the expansion of the arteries to such an extent as to cause occlusion of the cerebral veins, the volume of blood circulating through the brain is diminished. There follows under these circumstances what Grashey calls a vibration of the veins. The occlusion of the veins by the intracranial pressure is overcome by the consequent rise of static pressure transmitted through the capillaries, and this in turn is followed by occlusion as the pressure in the patent veins falls, and so on.

A similar view has been held by other authors who have treated the subject from a theoretical standpoint, and by some of those who have investigated the matter experimentally. The differences of opinion seem to be mainly as to the level of arterial pressure at which an obstruction to the blood-flow occurs, whether it falls within the range of normal variations of pressure or is reached only under extraordinary conditions. This admission appears to be of the nature of a theoretical concession to the recognized peculiarities of the cerebral circulation, and it is of interest to inquire how far it is supported by actual experiments. The simple and direct method of solving the problem is to measure the outflow of venous blood from the brain under different conditions of arterial pressure. This method has been employed by a number of authors with results which seem to be uniform and quite opposed to the conclusion obtained from a theoretical consideration alone. The experiments carried out by Gaertner and Wagner,[3] and since practically repeated by Bayliss and Hill,[4] Hill and Nabarro,[5] Reiner and Schnitzler[6] and others, have shown conclusively that the flow of blood through the brain is increased as the general blood pressure is raised. Even maximal blood pressures produced by the action of strychnine or absinthe give only an increased outflow from the cerebral veins with no indication of even a temporary slowing.

While these experiments have shown quite conclusively that a rise of blood pressure, so far as it can be produced by the normal regulating mechanisms of the circulation, fails to produce the condition of a diminished blood-flow as demanded by theory, it is held by some of the authors quoted that if the arterial pressure be still further increased, a point must be reached at which, owing to the compression of the cerebral veins, a permanent or temporary diminution of blood-flow will result. Thus Hill[7] says, "It is, however, possible that a very sudden and abnormally high rise of arterial pressure should so expand

the arteries at the base of the brain as to temporarily express capillary areas and produce anæmia."

It has been the object of my experiments to determine whether or not this is true. For this purpose I have used the simplest possible method. Upon dogs I have connected the arteries of the brain with reservoirs of blood, or Ringer's solution isotonic with the blood, that could be placed at any desired height, while the outflow from the brain was caught in a large test tube suspended by a spiral spring so that its movement, as it filled with blood, could be registered upon a kymographion. The details of the experiments were as follows: The animal was bled to death under ether. The internal carotids were dissected out and ligated. The vertebral arteries were exposed, and cannulas filled with defibrinated blood or isotonic salt solutions were introduced. These cannulas were connected with the reservoirs of carefully filtered calf's blood or Ringer's solution. In some cases the inflow cannulas were placed in the aorta or subclavians instead of in the vertebrals, and the flow directed into these latter arteries by ligating the other branches. To catch the outflow of blood from the brain, cannulas were placed directly in the superior cerebral veins at their emergence from the skull, or in some cases in the external jugular vein after ligating all communicating branches except the two superior cerebral veins. The internal jugular veins on the two sides were ligated close to the skull. An attempt was also made in some cases to shut off the outflow through the occipital sinuses into the spinal plexuses, but as this involved some danger of altering the conditions of pressure within the skull the attempt was abandoned. In the experiments as made, therefore, two paths of exit were opened to the blood flowing from the brain, — one, which was not measured, into the spinal plexuses, and one through the transverse sinuses and superior cerebral veins. The outflow from the latter was measured. This sufficed for the purposes of the experiment, inasmuch as in the dog this latter path is the one through which most of the blood escapes, and the object of the experiment was simply to determine the effect of very high arterial pressures upon the rate of outflow from the sinuses. The outflow cannulas from the two sides were united to a single short tube by means of a Y piece, and this tube opened into the test tube mentioned above. This test tube was provided below with an opening through which it could be emptied rapidly when desired. The tube was swung by a spiral of German silver wire after the manner sug-

gested by Bowditch for plethysmographic records, the spiral being so adjusted that the level of the liquid in the test tube remained constant. The movements of the tube as it filled with blood were recorded upon a kymographion upon which also a time record in seconds was taken simultaneously. As the movement downward of the test tube was constant and could be calibrated beforehand, data were obtained for calculating exactly the volume and the velocity of the outflow from the brain.

In performing an experiment two reservoirs were connected with the inflow cannulas; one of these was placed at a sub-normal level of from 30 to 60 mm. of mercury, while the other was at a height sufficient to cause a pressure of from 300 to 500 mm. Hg. The pinchcocks connected with the lower reservoir were first opened and the rate of flow was determined at this level. This pressure was then changed suddenly to the higher level by opening the pinchcock connected with the upper reservoir and closing the one on the tubing from the lower reservoir. The pressure was then brought back to the original amount by again making connections with the lower reservoir. The experiment was usually repeated a number of times. So long as the pressure was kept low, the rate of out-flow remained constant or nearly constant for some time, but exposure to the very high pressures brought about quickly an œdematous condition of the brain which diminished markedly the total outflow or might even suppress it entirely when the arterial pressure was subsequently lowered.

The direct results of the sudden change from sub-normal to supra-normal blood pressures were, however, the same in all cases; the venous outflow was increased at once to a proportional amount, and there was never any indication on the record of even a temporary blocking of the flow through the brain. The circulation through the brain under these conditions behaves in fact precisely as it does in the other organs of the body that are not enclosed in rigid cases.

The nature of the results obtained are indicated by the accompanying figures (Figs. 1 and 2) which are reproduced from the curves of two of the experiments. Examples of the actual amounts of outflow as calculated from the records are as follows: —

Exp. 1. Small dog — bled to death — blood defibrinated (140 c.c.) and mixed with equal volumes of normal saline and Ringer's solution to make 4 litres. Inflow cannulas placed in the vertebrals, outflow cannulas in the superior cerebral veins just at their emergence from the skull.

Arterial pressure of 30 mm. mercury = outflow of 7.02 c.c. per min.
" " " 60 " " = " " 18.03 " " "
" " " 380 " " = " " 102.60 " " "
" " " 60 " " = " " 10.24 " " "

2d series of observations on the same animal.

Arterial pressure of 60 mm. mercury = outflow of 9.65 c.c. per min.
" " " 400 " " = " " 85.14 " " "
" " " 60 " " = " " 5.85 " " "

Exp. 2. Small dog — bled to death from carotid — blood defibrinated (130 c.c.) and mixed with equal volumes of Ringer's solution and normal saline to make 5 litres. Inflow cannulas placed in the vertebrals, outflow cannulas in the external jugulars after ligating all branches except the superior cerebrals.

Arterial pressure of 30 mm. mercury = outflow of 5.26 c.c. per min.
" " " 122 " " = " " 34.52 " " "
" " " 30 " " = " " 2.22 " " "

2d series of observations on the same animal.

Arterial pressure of 50 mm. mercury = outflow of 2.57 c.c. per min.
" " " 375 " " = " " 70.2 " " "
" " " 50 " " = " " 1.17 " " "

Exp. 3. Large dog — bled to death from the carotids. For irrigating used freshly defibrinated blood of young calves filtered first through a single layer of muslin and then through four layers of the same. Inflow cannulas in the vertebrals, outflow cannulas in the superior cerebral veins at their emergence from the skull. Mercury manometers were also connected with the torcular and with the sub-dural space at the parietal eminence through trephine holes in the skull.

Arterial pressure of 60 mm. mercury = outflow of 23.4 c.c. per min.
A second determination 5 min. later = " " 22.23 " " "
Arterial pressure of 335 mm. mercury = " " 231.60 " " "
Rise of pressure in torcular cannula = 36 mm. of mercury.
" " " " cannula in sub-dural space = 30 mm. mercury.
Arterial pressure of 60 mm. mercury = outflow of 14.66 c.c. per min.

2d series of observations on the same animal — the flow meanwhile had diminished greatly, owing to leakage.

Arterial pressure 60 mm. mercury = outflow of 1.74 c.c. per min.
" " 460 " " = " " 252.72 " " "
Pressure in torcular increased 52 mm. mercury.
" " sub-dural space increased 20 mm. mercury. The want of correspondence between the intracerebral and torcular pressures was evidently due to the brain being forced into the trephine hole in the case of the former, thus blocking off the manometer.

Exp. 4. Small dog — bled to death from carotid. Irrigation liquid was blood of young calves carefully filtered. This blood had been kept over night and had frozen. This fact probably accounts for the unusually rapid diminution in flow as the experiment proceeded, the red corpuscles not passing readily through the capillaries and clogging them. Inflow cannulas in the subclavians, ligatures being so placed as to leave an open path only to the vertebrals; outflow cannulas in the superior cerebral veins at their emergence from the skull.

Arterial pressure 60 mm. mercury = outflow not measurable with accuracy.
" " 190 " " = " of 28.08 c.c. per min.
" " 320 " " = " " 47.38 " " "

2d series on the same animal.

Arterial pressure of 60 mm. mercury = outflow not measurable with accuracy.
" " " 400 " " = " of 42.12 c.c. per min.
" " " 500 " " = " " 50.02 " " "

FIG. 1. Record of venous outflow from brain under arterial pressures of 60 mm., 380 mm., and 60 mm.

Under 60 mm. Hg. the outflow = 18.13 c.c. per min.
" 380 " " " " = 102.66 " " "
Return to 60 " " " " = 10.24 " " "

The time record at the top of the illustration is in seconds.

It is evident from the data given that in all the experiments made, the blood-flow through the brain diminished as the experiment proceeded, and this effect was most marked after the blood vessels had been submitted to very high pressures. The probable explanation of this fact is that the dead capillary walls permitted a rapid filtration of liquid, which rendered the brain œdematous. This condition, in-

deed, was apparent to the eye when the brain was exposed after submission to the high intravascular pressures. This variation from normal conditions does not, however, affect the value of the experiments so far as the main point under investigation is concerned. The

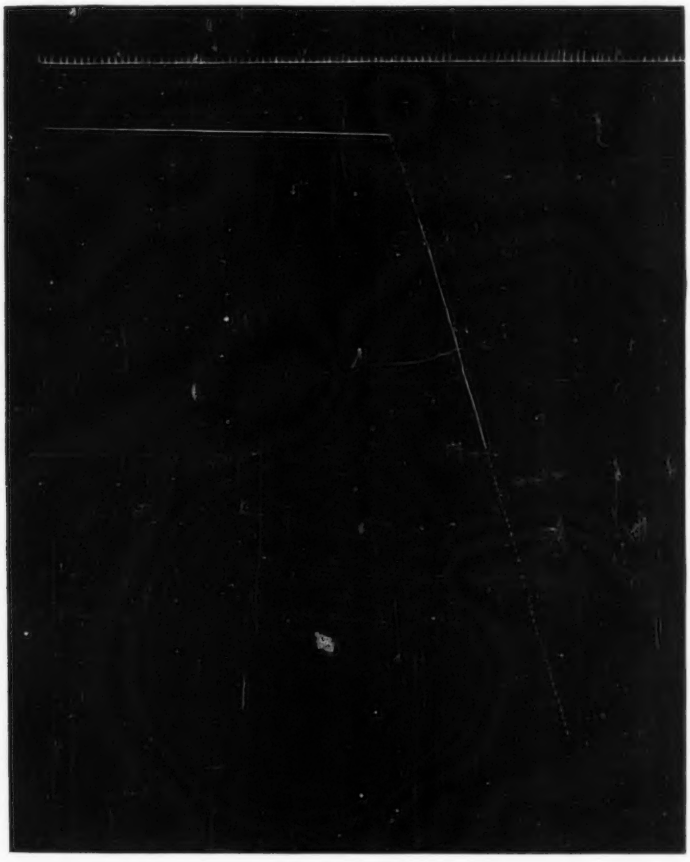

FIG. 2. Record of venous outflow from brain under arterial pressures of 60 mm. and 460 mm. (2d experiment.)

Under 60 mm. Hg. the outflow = 1.74 c.c. per min.
" 460 " " " " = 252.72 " " "

The irregularity in the beginning of the curve showing the outflow under 460 mm. arterial pressure, is owing to a stoppage of the drum, as will be seen by consulting the time record above it.

brain was still in the unopened cranium, and the physical conditions, which have been supposed to cause a compression of the veins and a temporary or permanent slowing of the blood-flow when the arterial pressure is suddenly raised to supra-normal levels, still prevailed. Indeed, the œdematous condition of the brain should have exaggerated this effect instead of counteracting it. Nevertheless, the records show that in all cases where the arterial pressure was suddenly raised to as much as 400 or 500 mm. of mercury, the outflow of blood from the cerebral veins increased promptly, and there was no indication at all of even a temporary blocking of the flow.

When we consider this fact, together with the results obtained by several authors upon the outflow in living animals in which the arterial pressure was raised by action upon the vaso-motor mechanisms, it seems justifiable to conclude that the blood-flow through the brain is always increased by a rise of arterial pressure, no matter how great or how sudden this rise may be, and that a compression of the veins sufficient to block or temporarily impede the blood-flow as a direct result of a sudden rise in pressure in the cerebral arteries is physically impossible. The author can indorse the conclusion drawn by Reiner and Schnitzler from their experiments that a rise of pressure in the cerebro-spinal liquid due to increase of arterial pressure cannot exceed the simultaneous intravenous pressure.

Obviously the authors who have arrived at an opposite conclusion have erred somewhere in the theoretical premises upon which their argument was based. A satisfactory treatment of all the physical factors involved in the statics and dynamics of the blood-flow through the brain is most difficult, and, perhaps, impossible in the present condition of our knowledge; but it seems to the author that in the theoretical considerations of the subject met with in physiological literature, some factors, which explain in large measure the contradiction between the experimental and theoretical conclusions, have been more or less overlooked. In the first place the view distinctly announced by some authors and tacitly assumed by others that arterial expansion causes a compression of the large venous sinuses of the brain seems to the author to be entirely inadmissible. Grashey calls attention to the anatomical facts that make this view improbable. The venous sinuses are covered by layers of the inextensible dura mater tightly stretched in some cases across bony channels. Any one who examines the

condition of these membranous walls in a fresh skull will be impressed with the opinion stated by Grashey, that the resistance to compression at these places must be so great, as compared with the cerebral veins that open into the sinuses, that any local or general increase of intracranial pressure must affect only the smaller veins. It seems to me, in fact, that the walls of the sinuses are practically incompressible, and that their existing structure is a beneficent adaptation to prevent any interference with the venous outflow arising from arterial expansion, since the venous system is thereby protected from compression at the point where its total cross area would be least, and intravascular pressure at its lowest, and where compression might most seriously affect the venous flow.

I have attempted to demonstrate experimentally the practical incompressibility of the large sinuses, but the method that I have used and which was the only one that seemed to be conclusive, developed so many technical difficulties that I have attained so far only partial success. The method was simple in idea, but somewhat difficult of execution. It consisted in first removing the brain entirely by washing out the tissue through the foramen magnum and a trephine hole in the parietal bone. A flexible rubber catheter was then taken, and upon one end was tied a delicate bag, made usually from the outer coats of the intestine of a frog. The catheter and bag were filled with water from a pressure flask so as to displace all the air, and the catheter was connected by tubing filled with water with a water manometer of barometer tubing. The catheter and bag were then introduced into the transverse sinus through the opening of the superior cerebral vein in the case of the dog, or through the internal jugular when the human skull was used. After the catheter was in position, the pressure in the water manometer connected with it was raised sufficiently to distend the bag and make it lie against the membranous walls of the sinus. Meanwhile the skull had been filled with water, the foramen magnum tightly closed off by a rubber stopper inserted in the sheath of the dura mater, and the trephine hole in the parietal bone connected properly with a mercury manometer and a pressure flask. By means of the latter the pressure within the skull was raised or lowered suddenly to any desired extent, and the effect of this variation in pressure upon the walls of the transverse sinus should have been indicated by the manometer connected with the catheter lying in the sinus.

The experiments of this character made upon human skulls were

not successful owing mainly to the fact that the skulls were obtained from cadavers used in the dissecting room, and the dura mater was so altered as to strip away easily from the bone. In the human skull also there is very great difficulty in getting the catheter through the internal jugular into the transverse sinus owing to the curvature of the channel. In the dog's skull the main difficulty lies in the fact that the transverse sinus throughout most of its extent lies in the bone, only a small portion of it near the torcular having a membranous wall. In other animals, such as the calf and sheep, the transverse sinuses have bony walls throughout their entire course. Another difficulty consists in the fact that the openings of the cerebral veins into the sinuses, particularly into the superior longitudinal sinus, are protected by dura mater so as to remain patent after washing out the brain, and thus make a free channel of communication between the skull cavity and the system of sinuses. This difficulty can be obviated by trephining into the torcular and closing off the sinuses with the exception of the transverse sinus used in the experiment. Still another obstacle is found in the fact that water will filter through the dura mater under high pressures, but the rise of pressure in the sinuses thus produced is gradual and quite different from the sudden rise which would occur if the walls of the sinus were compressed by a quick increase of pressure in the skull cavity.

In one experiment of this kind made upon the dog's skull — and in which subsequent dissection showed that the bag upon the end of the catheter lay properly in the membranous portion of the sinus, it was found that an increase in pressure within the skull up to 500 mm. of mercury caused not the slightest change in the level of the manometer connected with the catheter. This experiment seemed to show quite positively that the membranous walls of the transverse sinus cannot be compressed by intracranial pressures as high as 500 mm. of mercury. Unfortunately corroborative results could not be obtained upon the more favorable human skull owing to lack of appropriate material. But to the author's mind at least the anatomical structure of the sinuses and the physical characteristics of their walls are sufficiently conclusive in showing that normal or supra-normal variations in intracranial pressure cannot affect the calibre of these channels, particularly when we remember that the system of cerebral veins opening into the sinuses offers a relatively very low resistance to compression. As between the cerebral veins and the cerebral capillaries the lower internal pressure prevailing

within the former would seem to ensure that a general rise of intracranial pressure must affect the veins first.

With every increase in arterial pressure there is a tendency to the expansion of the cerebral arteries, but this expansion is only possible when a corresponding amount of liquid is forced out of the brain, the substance of the brain itself being practically incompressible. A clearer understanding of the conditions in the brain has led most authors to believe that room for a sudden expansion of the arteries is made in one of two ways, either by forcing out the cerebro-spinal liquid into the spinal cavity, or by a corresponding compression of the cerebral veins. With regard to the former of these two possibilities exact evidence is lacking of the extent to which it can compensate for arterial expansion, but the facts in our possession would seem to indicate that it plays a minor part. Hill has called attention to the fact that normally the quantity of liquid in the sub-dural and sub-arachnoid spaces is very small, and that under moderate expansion this is expressed into the spinal canal, where room is made for it by expansion of the vertebral ligaments and the possibilities of leakage through the sheaths of the spinal nerves. With a further increase of arterial pressure expansion becomes impossible unless there is a corresponding compression on the venous side, and, as we have seen, this compression should affect first the smaller cerebral veins.

That compression of these veins happens even before the cerebro-spinal liquid is entirely expressed seems to be proved by the occurrence of a pulse in the cerebral veins coincident with the arterial pulse. This venous pulse has been noticed by a number of authors. I have also observed and recorded it a number of times both in the outflow from the superior cerebral veins and from the torcular Herophili. It would seem that this pulse can be accounted for in one of two ways only. It is caused by a wave of pressure transmitted through the capillaries, or it results from a compression of the veins following upon arterial expansion. In the former case there should be a measurable interval between the time of appearance of the pulse in the circle of Willis and in the efferent veins; in the latter case the pulse should be practically simultaneous in the arteries and veins. To determine this point I have made simultaneous records of the pulse in the arteries and veins. The arterial pulse was measured in the circle of Willis by means of a Hurthle spring manometer connected with the head end of the internal carotid; the venous pulse was recorded by a delicate manometer constructed on the principle of

a Hürthle membrane manometer and connected with the torcular Herophili. This connection was made by means of a brass tube screwed into a trephine hole made into the torcular and filled with sodium carbonate solution.

A specimen of the record thus obtained is given in the accompanying illustration.

FIG. 3. Simultaneous record of the pulse wave in the torcular and in the circle of Willis (through the internal carotid). The upper curve records the pulse in the torcular, the lower that in the circle of Willis.

It was found that the two pulse waves occurred nearly simultaneously, and that in cases in which any difference in time was detectable the venous pulse slightly preceded the arterial pulse, the maximum difference in extreme cases being as much as 0.01 of a second. This difference is sufficiently accounted for by the stretch of elastic artery (internal carotid) extending from the circle of Willis to the point in the neck where the arterial manometer was inserted. These experiments seem to indicate that the venous pulse is not transmitted through the capillaries, but is due to a positive wave of pressure transmitted through the brain substance by the expanding arteries. This being the case it follows *a fortiori* that a greater general expansion of the arteries of the brain following upon a large rise of arterial pressure should be accompanied by a corresponding compression of the veins. This is the view that Grashey and others have taken, and that has led them to the apparently logical conclusion that a large rise of arterial pressure should result in a compression of the veins sufficient to occlude them temporarily and thus diminish the volume of the blood-flow. The experiments recorded in this paper, however, show that this conclusion is not justifiable. The venous outflow is not impeded even temporarily by a sudden rise of arterial pressure as great as 500 mm. of mercury. It remains for us to explain therefore this apparent discrepancy.

Granting fully that expansion of the arteries causes at once a rise of intracranial pressure sufficient to compress the veins, the fact that the blood-flow is not thereby momentarily impeded may be explained

by two considerations. In the first place in any vascular region the total cross area of the veins exceeds that of the arteries, so that an expansion of the arteries, if accompanied by a resulting symmetrical compression of the veins, would be distributed over a larger cross section and result in a relatively smaller diminution in calibre of the single veins. This consideration in the case of the brain is rendered more important, perhaps, by the fact that the venous system at its termination, namely, in the sinuses, is protected from external compression. The narrowing of the veins occurs, therefore, in the relatively wide area of the small veins, and although the total compression of the veins must equal the total expansion of the arterial stems, the narrowing of the single venous channels is slight, apparently too slight to cause a perceptible obstruction to the blood flow. In the second place the curve of extension of the elastic arterial walls under increasing pressures within follows the general law of extensibility for muscular tissue, showing a gradually decreasing extension for increasing increments of pressure. As the arterial pressure increases, therefore, the expansion of the arterial walls becomes rapidly less, the arteries approach nearer and nearer to the condition of rigid tubes, and the compression of the veins is correspondingly less important. These considerations suffice to explain why an actual occlusion of the veins, such as Grashey assumed, cannot possibly occur, and they explain also, perhaps, why not even a perceptible momentary blocking of the venous flow is obtained under normal and experimental conditions.

As to the permanent effects of arterial expansion upon the resistance to the flow in the veins, several authors have demonstrated quite clearly that even though the compression of the veins were sufficient to bring about a marked resistance to the blood-flow, this effect could only be temporary, inasmuch as the rise of static pressure within the capillaries and veins must always be more than sufficient to again expand the veins. Hill[8] has expressed this view in the following language: "The veins and capillaries, therefore, again become patent, because arterial pressure transmitted directly is obviously greater than arterial pressure minus the tension of the arterial wall transmitted through the brain substance." This author, however, admits that "if the cerebral arteries suddenly expand beyond a certain limit, a process of temporary self-strangulation of these vessels (veins and capillaries) takes place. The circulation itself for a short time stops, and the symptoms of acute cerebral anæmia are

produced." This conclusion, as I understand it, is based entirely upon theoretical grounds, and my experiments show that it is not correct, if it is assumed that the arterial expansion results from a rise of intravascular pressure.

The general conclusion, which seems to me to follow from the experiments given in this paper, is that *a rise of pressure, however great, in the cerebral arteries does not cause directly any impediment to the blood-flow either temporarily or permanently. The circulation in the brain behaves in this respect precisely as it does in the other organs of the body; the greater the arterial pressure the more abundant is the flow of blood, and temporary anæmia cannot be produced in this way.*

If it is found experimentally that a sudden great rise of arterial pressure causes an injurious effect upon the brain, this result cannot be attributed to the direct production of a temporary cerebral anæmia. We can imagine that under these conditions the functional activity of the brain might be interfered with for one of two reasons. It is possible, in the first place, that the resulting rise of intracranial pressure might affect the brain tissues directly; or, secondly, a rapid accumulation of lymph might take place within the brain, which, for a time, would impede the blood-flow, particularly after arterial pressure had again fallen. There is not much probability, however, that this latter effect could occur. Bergmann [9] found that injecting defibrinated blood at high pressures (800–1200 mm. Hg.) into the cerebral vessels of a horse caused no distinct increase in the lymph-flow, and several observers have shown that in other organs arterial hyperæmia alone is not necessarily followed by an increased formation of lymph.

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THE RECOVERY OF THE HEART FROM FIBRILLARY CONTRACTIONS.

By W. T. PORTER.

[*From the Laboratory of Physiology in the Harvard Medical School.*]

THE earlier experimenters on the coronary arteries described an apparently fundamental difference between the dog's heart and the rabbit's heart.[1] The heart of the rabbit was found to recover easily from fibrillary contractions brought on by the sudden closure of a large coronary artery, by mechanical injury, or by electrical excitation; but the dog's heart never recovered, either spontaneously, or when attempts at assistance were made by massage of the ventricle, stimulation of the ventricle with single induction shocks, or excitation of the vagus. The improbability of so great a difference between the hearts of two nearly related animals has not been able to outweigh the failure of these efforts to revive the dog's heart, and the idea that the heart of the rabbit and the dog are, in this respect, radically unlike, has obtained a wide acceptance.

It is somewhat strange that the belief in the fatal nature of fibrillary contractions in the dog should have become so fixed in the face of MacWilliam's positive statement that recovery can take place. Almost ten years ago MacWilliam,[2] in his refutation of Kronecker and Schmey's[3] hypothesis that fibrillation was caused by the destruction of a coördinating centre located in the interventricular septum near the junction of the upper and middle thirds, wrote as follows: "There is conclusive evidence that all cases of fibrillar contraction of the ventricle cannot be explained by such an hypothesis — the destruction of a coördinating centre localized as indicated above. The fact that recovery may take place — that the ventricles may resume their coördinated rhythm, controverts the idea of the actual destruction of a centre essential for coordination. Such recovery I have witnessed

[1] The literature of this subject is reviewed by W. T. PORTER, Journ. of physiol., 1894, xv, pp. 121–138; and Journ. of exper. med., 1896, i, pp. 46–70.

[2] MACWILLIAM: Journ. of physiol., 1887, viii, pp. 296–310.

[3] KRONECKER and SCHMEY: Sitz.-Ber. der Akad. d. Wiss. zu Berlin, 1884, p. 87.

in several instances in the dog's heart and in a very large number of instances in the hearts of other animals (cat, rabbit, rat, mouse, hedgehog and fowl). Recovery occurs with different degrees of facility in different animals and in different conditions in the same animal. In the dog, recovery occurs with much difficulty and only after the fibrillar contraction has lasted for a considerable space of time; indeed, there very frequently is no recovery apparent — the ventricle may not recommence beating after the incoördinated quivering movement has ceased. At times, however, a number of regular beats are seen after the termination of the fibrillar contraction. . . . In young mammals, fœtal or after birth, recovery appears to be the rule; the fibrillar movement is only a temporary condition, and soon gives place to normal beats" (p. 299).

The neglect of MacWilliam's observations by many subsequent writers is perhaps to be explained by their tacit assumption that fibrillary contractions produced by electrical excitation, — the agent used by MacWilliam for their production, — are not the same as those brought on by mechanical injury or by suddenly cutting off the blood-supply, so that recovery from the former does not necessarily prove the possibility of recovery from the latter. The experiments about to be described will show that this assumption has no foundation, and that the heart of the dog recovers from fibrillary contractions produced in any of these ways. It is true that recovery is much more easily obtained in the rabbit than in the dog, but the difference is merely in degree. There is, with regard to recovery from fibrillary contractions, no essential difference between the rabbit's heart and the dog's heart.

In pondering the cause of failure in the many previous attempts to resuscitate the heart, the following considerations became prominent. It is known that the continued coördinated contractions of the mammalian heart are impossible in the absence of a supply of blood to the cardiac muscle. It is also known that fibrillation arising from whatever cause must, by arresting the heart, cut off what has always been considered the only source of blood-supply to the cardiac muscle, namely, the circulation through the coronary arteries. The restoration of the circulation through the coronary arteries would seem, therefore, to be essential to the restoration of continued coördinated contractions; yet restoring the coronary circulation is a means of treatment that has thus far never been tried. The method of attack, then, should be to maintain an artificial circulation of

defibrinated blood through the coronary arteries of the fibrillating heart.[1]

But at this point it was remembered that the rabbit's heart often recovers spontaneously from fibrillation, although the arrest of the ventricle brings the blood-pressure in the aorta so low as to diminish greatly the circulation through the coronary arteries; and Mac William, as has already been said, saw even the dog heart recover spontaneously. How, it may be asked, can these hearts in which the coronary circulation was so much reduced have recovered without assistance, if the blood supply through the coronary arteries is so important to recovery? An answer to this pertinent question is furnished by two investigations recently made in this Laboratory, the first of which establishes the fact that the quantity of blood necessary for continued coördinated contractions is less than has been supposed, while the second demonstrates that this necessary quantity can be supplied to the ventricular muscle without the aid of the coronary arteries.

In the first[2] of these investigations the intraventricular pressure and the volume of the coronary circulation in the isolated heart of the cat were recorded simultaneously. It was found that the left ventricle would contract vigorously and for many minutes even when the coronary circulation was reduced to very low limits. The small blood-supply on which a good intraventricular pressure and a regular beat can be kept up is surprising. Reference to figure 1, plate 3 of the Paper in question, will show that admirable contractions were secured with about 3 c.c. per minute. In the experiment of March 13, 1896, fair contractions were seen with a coronary circulation of less than one cubic centimetre per minute; but this heart had been isolated a long time when the observation was made. These experiments are evidence that the mammalian heart will work with a blood-supply hitherto supposed to be wholly insufficient for contractions, even against little or no peripheral resistance.

The second[3] investigation shows this fact still more clearly, and shows beside that blood for continued, coördinated contractions can be obtained without the aid of the coronary arteries. In this research the right ventricle of the excised heart of the cat was kept contracting for several hours with no other blood-supply than that

[1] Porter: Journ. of exper. med., 1896, i, p. 69.

[2] Magrath and Kennedy: Journ. of exper. med., 1897, ii, pp. 13–34.

[3] Pratt: this Journal, 1898, i, p. 86.

obtained from the interior of the right ventricle through the vessels of Thebesius. The ventricle is tied firmly around a glass tube introduced through the pulmonary artery, the ligature passing below the auriculo-ventricular furrow and closing both veins and arteries. Defibrinated cat's blood is then poured into the tube until the ventricle is full and the blood stands in the tube at a height of one or two inches. The right ventricle will now begin to beat, and, if one of the coronary veins on the surface of the heart is incised, a slight but constant stream of blood will flow from the interior of the ventricle through the foramina Thebesii into the coronary veins and out of the opening on the surface of the ventricle. The blood becomes venous in its course through the heart walls. It has never been seen to enter the coronary arteries. Only that ventricle into which the blood is introduced has been observed to beat; the other ventricle remains inactive. Ringer's solution fails to maintain contractions. A ventricle that has fibrillated violently on the excision of the heart will often resume its coördinated contractions when a circulation is established in this manner through the vessels of Thebesius. Thus the nutrition of the mammalian heart may be maintained in a degree sufficient for long-continued, rhythmic contractions, while the coronary arteries are empty.

It should be observed that the state of the ventricle during fibrillation favors this mode of nutrition. Measurements taken in the left ventricle show that the intracardiac pressure rises at this time.[1] The heart becomes greatly distended. Meanwhile, the pressure in the aorta has fallen very low, the ventricle having ceased to beat, and, in consequence, the pressure in the coronary vessels is also very low. Hence the passage of the blood through the vessels of Thebesius into the coronary veins is doubly aided: on the one hand, by the relatively high pressure in the ventricle; on the other, by the diminished resistance in the coronary vessels. In the excised heart of the cat, an intraventricular pressure of two inches of blood will drive a constant stream through the vessels of Thebesius into the coronary veins, as has been already demonstrated, and the intraventricular pressure during fibrillation is probably greater than two inches of blood.

It should be noted further that the peripheral resistance against which the ventricle must work as it recovers from fibrillation is almost nothing, the arterial pressure having been enormously reduced

[1] PORTER: Journ. of physiol., 1894, xv, p. 132.

by the arrest of the ventricle. Thus the heart just recovering from fibrillary contractions and the heart removed from the body are very much alike in respect to the resistance against which the ventricle works. A difference in this resistance cannot, therefore, be urged against the conclusion that the blood-supply which keeps the isolated heart in rhythmic contraction will support the recovering ventricle until it can re-establish the circulation through the coronary arteries.

This same investigation has revealed yet another way in which the heart muscle may be nourished without the aid of the coronary arteries. On June 26, 1897, a cannula was tied into the distal end of the coronary sinus of the freshly extirpated heart of a cat, and filled with defibrinated cat's blood to a height of about 12 cm. Coordinated, regular, and complete contractions then began. The blood flowed from the coronary veins through the fine connecting vessels into the vessels of Thebesius and thence into the cavities of the heart, changing during its passage from arterial to venous. No blood was observed to enter the arteries. The contractions were facilitated by renewing the blood in the cannula from time to time. After twenty-five minutes the heart fell into pronounced fibrillation. Five minutes later the coordinated contractions were resumed, and continued with occasional pauses during almost half an hour. Again interrupted by fibrillation, they again returned, and both fibrillation and recovery were recorded graphically by a writing-lever attached to the apex. After several such attacks and recoveries the heart became exhausted and would beat no more.

The distension of the right auricle during fibrillation is even more favorable to the nutrition of the heart through the coronary sinus than is the distention of the ventricles and auricles to the nutrition through the vessels of Thebesius, for the coronary sinus is large and its valves are weak, falling back before the pressure of a few inches of blood and opening thus an ample way to vascular areas that may not, indeed, be truly capillary, but are none the less composed of vessels thin-walled enough to permit of nutrient osmosis; else why should the extirpated heart beat for hours when fed in this manner, and why should the blood that enters this path arterial red emerge a venous blue?

It is therefore a mistake to suppose that the feeding of the heart muscle is wholly interrupted by the failure of the circulation in the coronary arteries during fibrillation of the ventricle. A significant

supply is still possible. Usually this endocardiac nutrition, if I may term it so, falls below the required amount, and fibrillation continues to the end. In some instances, however, the endocardiac nutrition is sufficient, and the coördinated beat returns. But these unassisted recoveries are very rare, and all that we at present know seems to point to the advantage of liberally supplying the distracted muscle with defibrinated blood.

An artificial circulation of defibrinated blood through the coronary arteries of the fibrillating dog's heart was therefore established. My method of experiment was as follows: The animals were fully anæsthetized with morphia and ether, tracheotomized, the heart and blood vessels exposed by the resection of the first five ribs on the left, and the first three ribs on the right side, and a cannula placed in the left subclavian artery. The innominate artery was then ligated, and running nooses put around the aorta, just distal to the left subclavian artery, and around the ramus descendens and ramus circumflexus of the left coronary artery, near their origin. The cannula in the subclavian artery was connected to a Mariotte's flask of warmed defibrinated sheep or ox blood, placed high enough to give a pressure of 100 mm. Hg. in the aorta. All being in readiness, the nooses around the coronary arteries were drawn tight, until the heart fell into fibrillary contractions. These arteries were then freed, the noose around the aorta drawn tight, the stop-cock between the subclavian artery and the blood flask opened, and a large glass tube hastily tied into the pulmonary artery. The effect of these procedures was to cause the aorta to fill with sheep's blood at a pressure of 100 mm. Hg.; the semilunar valves being thereby tightly closed, and, every outlet but the coronary vessels being also closed, the blood passed through the coronary vessels into the right heart, whence it escaped out of the pulmonary artery into a dish. This blood was then beaten with a glass rod, filtered through glass wool, shaken with air to oxygenate it, and replaced in the Mariotte's flask.

Eight of these experiments were performed,[1] the first on March 7, 1896, and the last on April 23, 1896. The results were interesting, but not decisive. The character of the fibrillation was always modified by the making of the artificial circulation through the walls of the heart. The little contraction waves which cover the actively fibrillating heart were replaced by large undulations. In the experi-

[1] These experiments were done with the assistance of Mr. W. Tileston and Mr. E. DeW. Wales.

ment of March 21, 1896, these large undulatory movements became at times almost regular. On the whole, the impression made was that the ventricles were often on the point of resuming their coördinated contractions, but never altogether did so. Yet it seemed each moment that they would surely beat.

The hope of ultimate success was strengthened by several encouraging observations. The first was the success which attended the effort to restore coördinated contractions to the fibrillating auricle. Thus, in one dog, the heart began to fibrillate at 11.22 A. M.; the defibrinated blood was immediately turned on, and four minutes later the right auricle, which until then had been fibrillating like the rest of the heart, began to beat in an apparently normal fashion. The second encouraging circumstance was that occasionally, though rarely, a part of the ventricle would contract in a perfectly regular manner, while the remainder of the heart was still in hopeless confusion. The part which thus contracted was a small area in the right ventricle near the origin of the pulmonary artery. The third observation was made April 13, 1896. Pronounced fibrillary contractions appeared 215 seconds after the closure of the ramus circumflexus. The defibrinated blood was turned on, and in a short time movements which resembled feeble normal contractions were seen. Fifteen minutes after the beginning of fibrillation, the stop-cock between the blood reservoir and the aorta was turned off, and the supply of blood through the coronary arteries suddenly checked. Violent fibrillary contractions took place when the heart was thus deprived of its blood-supply. On restoring the circulation two minutes afterward, these gave way, and an almost normal beat returned. At the end of five minutes the circulation was again interrupted, and tumultuous fibrillation again appeared, thus showing that the amount of fibrillation was affected by the blood-supply. But notwithstanding these various signs that success was near at hand, no further progress was made at this time, and it was decided to wait until circumstances made it possible to feed the dog's heart with dog's blood.

While the experiments just described were making, other investigations,[1] on the isolated heart of the cat, afforded frequent opportunities to observe the easy recovery which the heart of that animal may make from fibrillation of long duration. When the isolated heart of the cat is fed through the coronary vessels with defibrinated cat's blood, the ventricles usually beat in a fairly normal fashion. Occa-

[1] MAGRATH and KENNEDY: Journ. of exper. med., 1897, ii, p. 14 and p. 30.

sionally, however, strong fibrillation sets in, very fatal to the hopes of the inexperienced operator. But if the experiment is faithfully continued, and the defibrinated blood kept flowing through the coronary vessels, the apparently hopeless ventricle often springs suddenly from its "delirium" into firm, coördinated beats. In one of the experiments published by Magrath and Kennedy, a cat's heart showed marked fibrillary contractions during forty-five minutes and then fell into regular, normal contractions, which continued more than an hour. It was difficult to believe that a disturbance often so transitory in the cat's heart should be always irrevocably fatal in the dog.

The recovery of the dog's ventricle from fibrillary contractions was finally accomplished during the experiments[1] which led to my discovery that any portion of the extirpated dog's heart, even the "ganglion-free apex," will usually resume its coördinated contractions when fed with the dog's own blood at the proper temperature and pressure.

On March 27, 1897, a dog weighing 10 kilogrammes, anæsthetized with morphia and ether, was bled from the left carotid artery, and the blood whipped, strained through glass wool, and diluted with an equal volume of 0.8% normal saline solution. Normal saline of the same strength, made with tap water, and having a temperature of about 36° C., was meanwhile allowed to flow into the right jugular vein. After a short interval the dog was again bled from the carotid artery. The product of these bleedings was mixed and placed in a reservoir at the temperature of the body. The heart was now extirpated, a cannula tied into the ramus descendens of the left coronary artery, the interventricular septum and the auricles completely cut away, and all the ventricle removed except that portion supplied by the descendens itself. The cannula was then connected to the reservoir of warm blood mixture, and the piece of ventricle perfused with the blood at a constant pressure, which to begin with was about 30 mm. Hg., but which was afterwards raised to 90 mm. Hg. The blood entering the cannula was bright arterial red; that emerging by the coronary vein was venous blue. In a few moments the ventricle began to beat with great vigor, shortening about seven millimetres in vertical diameter. An ordinary muscle lever, magnifying eight times, and weighted with 40 grammes, was fastened to a hook thrust through the apex, and recorded curves about 50 mm. in height. The curves showed some irregularity both in force and frequency. The ventricle

[1] PORTER: Journ. of exper. med., 1897, ii, pp. 391–404.

beat more rapidly when surrounded with blood at the temperature of the body than at room temperature, but the character of the contractions remained unchanged. At 1 P. M., after writing curves for one hour, the ventricle was thrown into fibrillary contractions by stroking its surface with the electrodes of a du Bois-Reymond induction coil (tetanic stimulation). Five minutes later good coordinated contractions returned. Forty minutes thereafter the ventricle was thrown a second time into fibrillary contractions, from which it soon recovered. Two and three quarter hours after the ventricle began to beat, the experiment was broken off. The contractions were by this time very feeble, but still unmistakably coördinated.

On March 29, 1897, a similar experiment was made, also on a dog. When the heart was removed from the body and the "apex" excised, the whole heart fell into fibrillary contractions. The right ventricle recovered from these without assistance, giving a few coordinated beats; the apex recovered on being fed with the defibrinated blood from the same dog, through a branch of the descendens. The apex was then thrown into fibrillation by stroking it with the electrodes of a du Bois-Reymond inductorium (hammer in action), but recovered speedily even when very strong currents were used.

The following day the heart of a dog was removed from the chest, and most of the left ventricle and all of the right ventricle and septum, except a fringe near the ramus descendens of the left coronary artery, were cut away. During the cutting of the heart, strong fibrillation appeared. A part of the right ventricle soon recovered spontaneously from this, giving a few fully coördinated beats.

On the afternoon of this day, in another heart, the part of the left ventricle supplied by the ramus descendens was fed through this vessel for nearly an hour without a pause in its ceaseless fibrillation, but finally a brief series of completely coordinated contractions was observed.

April 5, 1897, a still more remarkable recovery was noted. The part of the left ventricle (dog) nearest the apex was removed and fed through its coronary artery. The piece thus extirpated was 10 mm. in length. When good coordinated beats were secured, a powerful induction current was applied, throwing the perfused apex into fibrillation. Recovery took place in a few seconds. The current was at one time so strong as to burn the heart at the electrode points. The apex was now laid on one side in a beaker of blood. After about an hour, the apex was again perfused, and well coordinated,

but feeble contractions secured. Fibrillation was now easily produced with the induction current and continued a long time, but recovery at last took place.

Finally, in two cases, — the only ones in cardiac literature, so far as I am aware, — the dog's right ventricle fibrillated on its removal from the body, and yet, a moment later, unfed and undistended, gave a few coördinated beats. Continued contraction is of course impossible to the ventricle of the dog without a constant supply of nutrient material with which to replenish its rapidly impoverished intramolecular stores.

The experiments thus far related show that the cat's heart recovers readily from fibrillary contractions when the cardiac muscle is fed with the cat's own blood, and that various portions of the dog's heart, — for example, the auricle, the ventricle, and large parts removed from the ventricle, — will recover if fed with dog's blood; and they bring two cases of unassisted recovery, in which the dog's right ventricle, thrown into fibrillation by the extirpation of the heart, gave spontaneously, without perfusion of its coronary vessels, a few regular, coördinated contractions. They do not include any instance in which the whole dog's heart was recovered from fibrillation; but this is not to be wondered at, for the experiments in which the recovery of the whole heart was attempted were made with sheep or ox blood brought from the slaughter-house, and it is well known that such blood is injurious to the heart of the dog. I hesitated some time before attempting the recovery of the whole heart by the perfusion of dog's blood, for it was certain that two dogs would have to be used for each experiment in order to get sufficient blood for the satisfactory perfusion of the entire heart, and it was possible that many animals would be sacrificed to technical difficulties before a successful result could be reached. Moreover, additional experiments seemed unnecessary, for if the auricle and ventricle recover when separated, they should recover when left in their normal connection. This reluctance was strengthened by two preliminary trials, in each of which the whole dog's heart was fed with dog's blood, but without avail, owing to slight imperfections in method. It was therefore resolved to stop the fibrillation, if possible, before attempting to feed the heart muscle, in the hope that coördinated contractions would return if the perfusion was made after every trace of disordered contraction had disappeared. The entire success of this plan is shown by the following experiments.

Experiment Oct. 25, 1897. A large dog, anæsthetized with morphia and ether, was bled, perfused with 0.8 per cent sodium chloride solution, bled again, and the blood defibrinated and placed in a pressure-flask at the temperature of the body. The heart of a small dog, anæsthetized with morphia and ether, was then exposed, and the venæ cavæ, the right vena azygos, the aorta, and the innominate and left subclavian arteries ligated. Cannulas were placed in the innominate artery, the pulmonary artery, and the two auricles. The cannula in the innominate artery was connected with the pressure-flask, and supplied the coronary arteries with blood, which, after passing through the heart muscle, escaped from the coronary veins and the vessels of Thebesius and found its way out of the heart by the cannulas in the pulmonary artery and auricles. As soon as the warm defibrinated dog's blood was forced through the coronary vessels, the heart, which had ceased to beat while the preparations were making, began to contract in its regular, normal way. Fibrillation of both auricles and ventricles was now induced by stimulating the ventricles and auricles with a rapidly interrupted current from a du Bois-Reymond inductorium. The auricles soon recovered their coördinated contractions, but the ventricles continued to fibrillate for a little more than an hour. The supply of blood to the heart was then cut off, and iced normal saline solution poured upon the heart until every trace of fibrillation had ceased. The coiled bulb of a surface thermometer placed on the ventricle gave a temperature of 22°C. Blood at 36°C. was again allowed to flow through the coronary arteries. The whole heart then began to beat. The contractions were feeble, but entirely regular and fully coördinated.

Experiment, November 3, 1897. The heart of a dog anæsthetized with morphia and ether, was perfused with warm defibrinated dog's blood, as in the preceding experiment. The heart beat very well as soon as the perfusion began. Fibrillation was now brought on by electrical stimulation. The perfusion was then stopped, and iced saline solution poured over the heart until all movement had ceased. On again perfusing the heart with blood at 36°C., thoroughly good contractions, strong, regular, and perfectly coördinated, began. After this strong and regular beating had been watched for some time, fibrillation was again induced, and the heart cooled down, as before. But perfusion was this time recommenced before the last tremor had ceased. The result of this premature action was the return of fibrillary contractions in full force. Twice again the heart was cooled and perfused before fibrillation had wholly ceased, with the same result. Then still another cold bath was given, and this time perfusion was not begun until the ventricle lay quiet. The heart now beat in normal fashion for a long time, the contractions being very forcible and completely coördinated.

Thus the whole dog's heart can be recovered from fibrillary contractions by cooling the ventricles until all trace of fibrillation has disappeared, and then bringing the heart back to the normal temperature by circulating warmed defibrinated blood through the coronary vessels. Doubtless the whole heart of the dog, like the auricles and ventricles, and like the heart of the cat and the rabbit, can also be recovered by persistent feeding with defibrinated blood at normal temperature and pressure, and, in very rare cases, by endocardiac nutrition through the vessels of Thebesius and the coronary veins, but further experiments would only confirm the statements contained in these pages. The thesis with which this Paper began has been sufficiently demonstrated. In respect of recovery from fibrillary contractions, there is no essential difference between the hearts of the rabbit, the cat, and the dog.

NOTES ON THE ELIMINATION OF STRONTIUM.

By HORATIO C. WOOD, Jr., M. D.

[*From the Chemical Laboratory of the University of Pennsylvania.*]

IN H. C. Wood's Therapeutics it is affirmed that the absorption of the strontium salts and their elimination *appears* to be rapid, but the only exact chemical studies of the matter which I have been able to find are those of Laborde, Compte rendu de la Société de biologie, Paris, 9 s., 1890, vol. ii, pp. 453 and 708, and 1891, vol. iii, p. 562. In one of Laborde's experiments an amount of the strontium sulphate sufficient to represent 117 gm. of the metallic strontium was administered to a dog by the mouth in the course of 81 days, and the metal was found in the urine, fæces, bones, and liver. In a second experiment, the tartrate having been given in such quantity as to represent 453 gm. of the metallic strontium, that substance was again detected in the urine, bones, and liver, but was especially abundant in the fæces. In a third experiment, strontium phosphate representing 265 gm. of the metal was given in 111 days; in the urine and liver only unweighable traces were found, — from the bones was separated 0.63 gm. of the metal. Except in regard to the bones in the last experiment mentioned, Dr. Laborde does not report any amount of weighed metal obtained.

These experiments of Laborde do not prove that strontium is rapidly absorbed or eliminated, but only that it is absorbed to some extent and slowly rather than rapidly thrown off. For the purpose of obtaining more exact data I have made two experiments. The method of separating the strontium, for which I am indebted to Professor John Marshall, is as follows: —

"The urine and fæces were separately evaporated to dryness, and the residue incinerated until the organic matter was completely destroyed. The residue was warmed with nitric acid, the solution diluted with water, filtered, the filtrate nearly neutralized with ammonium hydroxide, and ammonium carbonate added in slight excess. The liquid was boiled, and the precipitate collected on a filter paper and thoroughly washed. The precipitate was then dissolved in just sufficient acetic acid to bring it into solution, and the solution then diluted with water. To remove phosphoric acid ferric

chloride was added and the solution nearly neutralized with sodium carbonate. The liquid was boiled, and filtered while hot to remove the triferric phosphate and basic ferric acetate which had separated. The filtrate was evaporated to dryness on a water-bath, and the residue repeatedly treated with nitric acid, evaporating the solution to dryness after each addition of nitric acid to convert the calcium and strontium present into nitrates. The dry residue was pulverized and treated with a mixture of strong alcohol and ether to separate calcium nitrate from strontium nitrate. The residue remaining after treatment with strong alcohol and ether was tested by means of the flame test for strontium, and wherever the quantity of residue remaining indicated a weighable quantity of strontium the residue was dissolved in a small quantity of water and the strontium precipitated by the addition of dilute sulphuric acid. In such cases the liquid was permitted to stand 12 hours, when the precipitate of strontium sulphate was collected on a filter paper, washed with a mixture of alcohol and ether, dried, incinerated, and weighed."

The first experiment was upon myself. In it I took by the mouth 3 grammes of strontium lactate ($Sr(C_3H_5O_3)_2$) representing 1.89 grammes of metallic strontium. The urine and fæces were collected separately for forty-eight hours. The result may be presented conveniently in a tabular form as follows: —

First day.

9 a. m. Ingestion of 3 gm. strontium lactate.
10 a. m. Urine contains a trace of Sr.
2 p. m. " " " "
6 p. m. " " " "

Second day.

9 a. m. Fæces contain 0 0223 gm. metallic Sr.
2 p. m. No strontium in urine.
10 p. m. " " "

Third day.

9 a. m. Fæces contain 0.1503 gm. metallic Sr.

Unfortunately the fæces were not saved after the third day, but it will be noted that during the forty-eight hours after the ingestion of an amount of strontium lactate representing 1.89 grammes of the strontium, 0.1706 gramme of the strontium was recovered from the fæces, equalling about 10 per cent of the amount ingested, whilst only a trace was found in the urine. This result is capable of several explanations; it is possible that the strontium is not absorbed and very slowly passes out from the alimentary canal, owing to its weight

causing it to cling to the mucous membranes; or it is possible that being more largely absorbed than is apparent it is eliminated with great slowness. The latter conclusion, however, is highly improbable in the face of the fact that the strontium disappeared from the urine within twenty-four hours. If absorption and retention were the case, certainly there should have been as much strontium in the urine on the second as on the first day. It is of course possible that the discharge of strontium with the fæces may have depended upon an elimination of absorbed strontium by the intestinal mucous membrane.

To determine whether such elimination occurs to any extent a second experiment was made. In this a small dog was given a hypodermic injection of 3 grammes of strontium lactate, dissolved in water. The urine and fæces were separately collected for 72 hours, and carefully examined by the process previously given, but no strontium was detected.

The experiment just recorded shows that strontium given hypodermically, if absorbed at all, is only eliminated with the greatest slowness; and demonstrates that the strontium which was passed from the bowel in the first experiment had not been eliminated from the bowel but had remained unabsorbed. As suggested by Professor Marshall, it is probable that when the strontium salt is taken by the mouth absorption takes place to some extent in the stomach, but that that portion of the salt which escapes into the intestines is converted into an insoluble phosphate. It is also probable that the alkaline juice of the tissues largely breaks up the strontium salt, so that absorption from the cellular tissue is a very slow process. It is a further plausible conclusion that the strontium salts taken into the intestines, like the bismuth salts, are so very slowly absorbed that they exert a persistent local influence; an experimental conclusion which is in accord with the clinical fact which has been insisted upon especially by Professor H. C. Wood, that the strontium salts have a marked influence upon the digestive processes in the intestinal canal.

PHILADELPHIA, *August*, 1897.

THE NUTRITION OF THE HEART THROUGH THE VESSELS OF THEBESIUS AND THE CORONARY VEINS.[1]

By F. H. PRATT.

[*From the Laboratory of Physiology in the Harvard Medical School.*]

FEW beliefs of the present day are more firmly intrenched than that of the total dependence of the mammalian heart upon the coronary arteries. We are taught that without the blood brought by these vessels the long-continued, rhythmic contractions of the cardiac muscle are impossible. Such is the foundation on which rest in large part the prevailing ideas of infarction in the heart, with all the train of evil consequences believed to follow the embolism and thrombosis of the coronary arteries. It is my purpose to show that this doctrine is not absolute. The long-contracting, rhythmic heart is not wholly dependent upon the coronary arteries for its food supply; on the contrary, the heart will beat for hours while its arteries are empty. There are two ways in which the heart muscle may thus be nourished: the first, through the vessels of Thebesius, which open from the ventricles and auricles into a system of fine branches communicating with the cardiac capillaries; the second, through the coronary veins, which may convey a backward flow of blood from the auricle into the tissues of the heart.

So far as I have been able to determine, no experimental physiological work has ever before been done on the vessels of Thebesius; all opinion regarding their functional importance has rested upon the assumption that they serve only as veins, conveying a part of the venous blood from the coronary capillaries through the foramina Thebesii into the cavities of the heart. The question, too, of the nutritive significance of regurgitation from the auricle into the coronary veins has not apparently at any time been the object of investigation.

[1] The first account of these experiments was given to the American Physiological Society in May, 1897 (see Science, June 11, 1897). The subject was presented also to the Boston Society of Medical Sciences, June 1, 1897, and to the British Association for the Advancement of Science, Toronto, August, 1897

The following pages will present an historical sketch of the anatomy of the vessels of Thebesius, and a record of my own anatomical studies of these vessels and of the coronary veins; a detailed account of my experiments on the nutrition of the heart through the vessels of Thebesius and the coronary veins will follow; and, finally, I shall endeavor to show that these forms of nutrition afford a reasonable explanation of the recovery of the heart from fibrillary contractions and from acute distentions leading to arrest, and of the extraordinary fact that hearts may work for years in spite of the almost complete obstruction of their arteries by advanced arterio-sclerosis.

I. The Anatomy of the Vessels of Thebesius and the Coronary Veins.

The Vessels of Thebesius. — The discovery of the foramina Thebesii is credited to Vieussens;[1] but we owe the first accurate description of them to Thebesius,[2] whose valuable work, *De circulo sanguinis in corde*, was published by A. Elzevier in 1708. Nearly fifty years later we find Haller[3] describing "still more, and much smaller, veins in the heart, whose little trunks, being very short, cannot easily be traced by dissection; and these open themselves by an infinite number of oblique small mouths, through all the numerous sinuosities observable on the surface of the right and left ventricle. These are demonstrated by injections of water, wind, or mercury, pushed into the coronary arteries, after you have first tied their corresponding or accompanying coronary veins; or even into the great coronary veins, after you have first intercepted the openings of their largest trunks. For, in either of these cases, there are drops of the tinctured water, bubbles of air, spherules of mercury, rushing out through the whole extended surfaces of both ventricles of the heart; and this, without any violence that can be supposed sufficient to break the vessels. But the passage from the arteries into the cavities of the left side is more difficult." Notwithstanding these various statements the existence of the vessels remained for many years a subject of dispute. Thus Abernethy[4] early in the present century, commenting

[1] Vieussens: Nouvelles découvertes sur le cœur: 1706; quoted by Haller: Elementa Physiolog. Lausanne, 1757, lib. iv, p. 380.

[2] Thebesius: De circulo sanguinis in corde. Leiden, 1708.

[3] Haller: First lines of physiology: English translation. Edinburgh, 1786, vol. i, p. 75.

[4] Abernethy: Philosophical Transactions. London, 1798, p. 103.

on the perplexities of his predecessors, pointed out that even Haller, Senac, and Zinn were sometimes unable to discover the foramina, and were led to suspect that their apparently successful injections really ruptured the vessels and forced a way through false passages into the cavities of the heart. Abernethy himself made many injections, filling the arteries and veins with wax of different colors. He convinced himself that the foramina actually existed; and that they belonged moreover to both the arteries and the veins, because "the injection which was employed was too coarse to pass from one set of vessels to the other, and yet the different coloured injections passed into the cavities of the heart unmixed." His conclusion that some of the foramina communicate with coronary arteries is, I think, hardly to be accepted in the light of other observations. It is probable that in his experiments also extravasations took place from the arteries into the ventricles.

Bochdalek,[1] in 1868, published the results of observations on the foramina Thebesii of the auricles. He found in both auricles the mouths of small vessels. Many of these openings presented the appearance of blind depressions, since they were often covered with single valves in such a way as to resist investigation with the blowpipe. When he succeeded in introducing an injection-mass or a blast of air into a foramen, superficial, ramifying vessels were demonstrated, the injection of which often showed a connection with other foramina in the same auricle, or even in that of the other side. The foramina varied considerably both in number and in size; some were round and small; others were slit-like, resembling the mouths of the ureters; still others were large, round depressions, with smaller openings at the bottom. As a result of his observations, Bochdalek concludes "that the greater number of the small openings on the inner surface of the right as well as the left auricle, which from early times have borne the name of foramina Thebesii, represent the mouths of little veins that, often uniting into larger vessels, course with many branches through the auricular walls."

In 1880 appeared the report of Langer's[2] research on the foramina Thebesii of the human heart. With the aid of the blowpipe, and by means of a watery injection mass colored with Berlin blue, he demonstrated these foramina in all the cavities of the heart. He

[1] BOCHDALEK: Arch. f. Anat., Physiol. u. wiss. Med., Leipzig, 1868, p. 314.

[2] LANGER: Sitzb. der k. Akad. der Wissensch. zu Wien, 1880, Bd. lxxxii, 3. Abth., p. 25.

succeeded in injecting the vessels of Thebesius not only from the coronary vessels, but from the endocardial surfaces as well. Hochdalek's observations regarding the presence in both auricles of foramina Thebesii were thus confirmed, and the fact of a communication between the coronary vessels and each of the four cavities of the heart was thoroughly established. The foramina which Langer found on the endocardial surfaces of both ventricles were similar to those in the auricles, but much smaller. They were most conspicuous on the papillary muscles and in the neighborhood of the great vessels, being less easily seen in the region of the apex, where they were obscured by the trabecular network. Injections from the endocardial surfaces showed fine, ramifying vessels connected with the foramina, running either at right angles to the surface, or obliquely. From the fact that thick injection masses would not pass from the coronary veins into the ventricles, and that even watery masses were slow in appearing there, Langer concluded that the foramina Thebesii of the ventricles were not, as occasionally happens in the auricles, in direct communication with the coronary veins, but that they had to do with separate capillary areas. In no case did he observe valves in connection with the foramina Thebesii of the ventricles.

Gad[1] has recorded some confirmatory observations on the vessels of Thebesius in the ox. In the method which he describes for demonstrating the action of the valves of the left heart, wherein water under pressure is made to fill the ventricle and aorta, he noticed that water flowed into the right heart from the foramina Thebesii. On illuminating the interior of the left ventricle he was enabled to see fine, blood-stained streams, issuing from the endocardial wall into the clear water with which the cavity was filled.

Finally, Magrath and Kennedy,[2] working with artificial circulations of defibrinated blood on the isolated heart of the cat, observed that a small portion of the coronary blood found its way into the left ventricle. The only possible source of access, other than from the vessels of Thebesius, was leakage past the aortic valves. This leakage, as shown by a manometer record of the aortic pressure, did not occur.

Notwithstanding these painstaking observations, the vessels of Thebesius still occupy a very obscure position in anatomical literature. Foramina Thebesii are referred to as constant in the right

[1] Gad: Arch. f. Physiol., 1886, p. 380.

[2] Magrath and Kennedy: Journ. of Exp. Med., 1897, ii, p. 13.

auricle, forming in part the mouths of small veins. Their occurrence in the left auricle is occasionally mentioned. But the fact that vessels of Thebesius open into all the chambers of the heart — ventricles as well as auricles — is hardly recognized.

The anatomical methods employed in the present study have been three in number; the injection of the vessels with air by means of the blowpipe, their injection with liquids, and the making of corrosion preparations. My experiments have in the main confirmed the results of other observers.

The initial step was to demonstrate independently the fact of a circulation in the vessels of Thebesius. By the injection of water, normal saline solution, or defibrinated blood, at a constant pressure, I established an artificial circulation through the coronary vessels of the fresh, often the still living, extirpated hearts of the rabbit and the dog. The cannula was tied directly into a coronary artery or one of its branches, so that access of liquid into the heart-cavities, except through the endocardial foramina, was rendered impossible. Yet liquid constantly found its way through the vessels of Thebesius. Thus I was enabled to verify the results of Magrath and Kennedy touching these vessels. It is essential to success that the heart be used before rigor has set in, and that the coronary system be thoroughly washed out by the injection of water or normal saline solution into the aorta. The following experiment will make the procedure clear.

February 8, 1897. A dog was anæsthetized with morphia and ether, and the heart excised after contractions had ceased. The coronary system was rinsed with normal saline solution introduced from the aorta. The systemic and pulmonary veins and the right coronary artery were ligated. A cannula was passed into the left coronary orifice from the aorta, and tied in the descending branch of the left coronary artery. The walls of the aorta were drawn close to the shank of the cannula by a ligature. Two outflow tubes were now arranged; one in the right ventricle through the pulmonary artery, the other in the left ventricle through the left auricular appendix. Normal saline solution colored with defibrinated blood was passed through the cannula under a constant pressure of 85 mm. Hg. and collected from each outflow tube separately. The amounts were then measured and compared. The quantity of the solution collected during five minutes was 400 cc. from the right ventricle, and 4 cc. from the left.

After thus assuring myself that a genuine communication exists between the coronary vessels and the left heart, it remained to in-

quire particularly into the nature of this communication. The heart of the ox was found best suited to the purpose. An examination of the endocardial surfaces of the ox heart reveals irregularly placed depressions, usually sharply outlined, varying widely in size, shape, and distribution. They are regularly larger in the auricles than in the ventricles. In the right auricle they may be provided with thin, single valves, especially about the origin of the great veins. In the left auricle they are usually fewer in number, and, so far as my observations have gone, unprovided with valves. Foramina Thebesii are never absent from the ventricles. In the right ventricle, which is especially well provided with them, the larger number are seen upon the septal wall. It is often much more difficult to find them in the left ventricle, although a diligent search is never without reward. Here, in agreement with Langer's statement, they often appear at or near the bases of the papillary muscles. They may present themselves in either ventricle almost anywhere on the endocardial surface. Structures, accessory to these ventricular foramina, which might in any way serve the office of valves, I have not seen; the edge of the foramen is usually sharply defined and may frequently exist as a partial, shelf-like covering, giving the impression, perhaps, of an attempt at a membranous valve; but it is seldom more than this.

Experience soon teaches one to distinguish, often at a glance, between the foramina Thebesii and merely blind depressions in the endocardium. On the injection of the vessels of Thebesius with air by means of the blowpipe applied to the foramina, characteristic, fine, sub-endocardial ramifications, which very frequently conduct the air into other Thebesian systems or even into the great coronary veins, will seldom fail to appear. Connection with the coronary veins may be further established by injection from the veins themselves. The following observations will illustrate these points.

April 7, 1897. — The right ventricle of a fresh ox heart was opened from the tricuspid valve to the apex. A large number of foramina were seen on the septal endocardial wall. The inflation with the blowpipe of vessels leading from these was in most instances followed by the appearance of air-bubbles at the mouth of the coronary sinus. On tracing the source of the bubbling, the air was observed to come from the mouth of a coronary vein at the extreme end of the sinus. This vein was now opened, and a cannula tied into the distal end. Defibrinated blood, forced through the cannula by blowing into the end of an attached rubber tube, was plainly seen to emerge from the foramina.

The ease with which injections of air and blood could be made to demonstrate the connection between the vessels of Thebesius and the coronary veins caused me to doubt the opinion expressed by Langer, that the foramina Thebesii in the ventricles communicate with the veins by capillaries alone. To settle this point I injected the coronary veins of the ox with starch and celloidin masses, both too thick to pass the capillaries, and found that even these emerged from the foramina Thebesii of the right ventricle. So intimate a connection, however, between the coronary veins and the vessels entering the left ventricle I have not yet been able to demonstrate.

By means of a very successful corrosion preparation, made by injecting the veins of an ox heart with celloidin, I was able to trace the communication. In this preparation the position of some of the foramina Thebesii was marked by small discs of the hardened mass, formed by the oozing out of the celloidin upon the endocardium. These foramina were shown to be connected with the smaller coronary veins by fine branches. The still finer ramifications which, as Langer has demonstrated, lead from the foramina and branch directly into capillaries were here uninjected; they would appear only when injected from the foramina themselves.

Although I have made attempts, I have been unable to discover anything more free than a capillary connection between the vessels of Thebesius and the coronary arteries. Injections of starch or celloidin fail to pass from the arteries into the cavities of the heart.

Bochdalek's observation, relative to a communication between the auricles through vessels of Thebesius, I have verified on the heart of the dog. Blowpipe injection of a foramen in the left auricle caused an exit of air from a similar foramen in the right auricle, and this without any discernible inflation of a coronary vein.

I have no reason to believe that any of my results have been due to the rupture of vessels and the consequent extravasation of the circulation-fluid or injection-mass. Care has been taken throughout to avoid high pressures, and this, together with the very important consideration that my material has all been fresh, would serve to render errors resulting from this cause very improbable.

The vessels of Thebesius, therefore, open from the ventricles and auricles into a system of fine branches that communicate with the coronary arteries and veins by means of capillaries, and with the veins — but not with the arteries — by passages of somewhat larger size.

The Coronary Veins. — Whenever in my experiments a circulation-fluid has been permitted to gain access to the coronary sinus from the right heart, the anatomical possibility of a back-flow into the veins has been demonstrated. I have taken pains to supplement these observations with dissections of the coronary veins in the cat, dog, and ox. Everything has pointed to the fact that such valves as the veins of the heart possess are very inefficient. A single membranous fold is usually found at the entrance of a vein into the sinus; seldom does it prevent the entrance of air or liquids. Valves at the confluence of venous branches I have found either wanting or very poorly developed. The Thebesian valve at the mouth of the coronary sinus is totally insufficient to prevent regurgitation.

II. The Nutrition of the Heart through the Vessels of Thebesius.

The experiments which I shall now describe were suggested by the possibility of an arterial function on the part of the vessels of Thebesius. They have served to prove not only that these vessels may carry nutriment to the heart-muscle, but that in the absence of all other forms of cardiac nutrition — with the blood-supply through the coronary arteries absolutely cut off — the mammalian ventricle may be maintained, under proper conditions, in rhythmic contractions lasting several hours.

Nearly all of the experiments have been made upon the heart of the cat. The animal is anæsthetized with ether, tracheotomized, and bled from a cannula tied into a carotid artery. The blood is defibrinated and filtered through glass wool. On cessation of the bleeding the ventral chest wall is at once removed by cutting through the costal cartilages, and the heart quickly severed from its connections. If care has been taken with the etherizing, respiration should have persisted up to the time of opening the thorax, and the excised heart should be beating with perfect regularity; fibrillary contractions need not, however, interfere with success. The heart is rinsed in warm normal saline solution. A cannula about the size of the aorta is now introduced into the right ventricle through either the auricle or the pulmonary artery, and secured by a ligature passed tightly around the base of the heart in a line parallel to the auriculo-ventricular groove and below the coronary sinus. Thus a fluid introduced into the ventricle through the cannula can find no outflow except through the vessels of Thebesius. The cannula is now supported in an

upright position, with the heart suspended from the lower end, and the defibrinated blood poured in until the ventricle is full and the blood rises in the tube to a height of several inches. Figure 1 will make clear the relation of the cannula to the ventricular cavity. Figure 2 represents a form of perfusion cannula and a heating apparatus which have been found very convenient for supplying fresh blood constantly to the ventricle, and for maintaining the heart at body-temperature.

FIGURE 1. Diagram to illustrate the mode of securing the cannula in the ventricular cavity for nutrition through the vessels of Thebesius.

As a result of the above method — often within a minute after the introduction of blood — strongly marked, regular, coördinated contractions of the ventricle are observed. With a periodic supply of fresh blood, and with favorable temperature and moisture, this activity may continue several hours. The following are typical experiments.

April 1, 1897. An etherized cat was tracheotomized and bled from the left carotid artery. The heart was excised while beating, and rinsed in saline solution. A cannula was passed into the right ventricle through the right auricular appendix, and secured by a ligature tied tightly about the base of the heart. The heart had fibrillated immediately after excision, and shortly had ceased all movement. The cannula and the ventricle were now filled with defibrinated blood diluted with one part saline solution. The ventricle straightway began to beat with great regularity. On suspension of the heart in saline solution of normal temperature the beat was increased in frequency. The blood, rising in the tube about 15 mm. with each beat, became gradually venous in color. The frequency of contraction then diminished, but was restored by replacing the venous with arterial blood. No diminution in the amount of the blood was noticeable, and no blood could be seen to issue from the heart. The coronary arteries were empty; the veins were filled over the entire surface. Tracings were taken by attaching a rubber tube connected with a Marey tambour to the top of the cannula (Fig. 3). The resistance thus occasioned gradually lessened the frequency of the heart-beat, but the heart immediately recovered its former rate on removal of the tambour-tube.

The heart began beating at 4.55 P. M. At 6.20 it was still beating slowly. The blood had been renewed several times.

An experiment of April 2, 1897, showed that a true circulation may take place between the vessels of Thebesius and the coronary veins. Here the conditions were the same as in the experiment just

recorded, except that two of the veins were incised. A small but steady stream of venous blood issued from them.

On April 3, under the same conditions, the descending branch of the left coronary artery was opened. No flow of blood occurred from the artery, although there was a free escape from an incision in an accompanying vein.

The following experiment shows that the above form of nutrition is not confined to the right ventricle.

April 7, 1897. The left ventricle of a cat was nourished with blood by the same method, except that the trunks of both coronary arteries were ligated, and the ligature about the ventricles omitted. The supply cannula was tied into the ventricle through the aorta. On the introduction of blood the left ventricle alone began to beat strongly and regularly. The height of the blood column was about 80 mm. A small but continuous flow of blood occurred from a cut vein. The beating continued for over an hour, becoming weak at last, but remaining regular. The blood found its way in part into the right ventricle, coming of necessity through the walls. The blood had been changed frequently by perfusion, and had invariably become venous in color. The temperature was kept at 30–36° C.

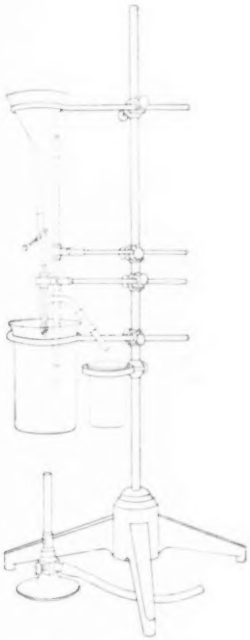

FIGURE 2. Perfusion apparatus for feeding from the interior of the heart-cavities. Blood placed in the funnel is allowed to pass very slowly through the fine glass tube into the ventricle, which is tied upon the cannula as illustrated in Figure 1. The supply is regulated by the compression clamp. Each beat of the ventricle forces the blood back through the space between the fine inner tube and the walls of the cannula, out through the side branch, and thence into the small receiving beaker. The large beaker is filled with saline solution kept at normal temperature.

In considering these experiments the suspicion very naturally arises that the prolonged contractility of the filled ventricle may be due, not to the nutritive property of the blood, but to mere mechanical stimulation brought about by distention. Evidence that such distention is in itself a powerful stimulus to contraction has recently been furnished in this Labo-

ratory.[1] But mechanical stimulus is inadequate to explain the phenomenon; for when Ringer's solution of sodium, potassium, and calcium chlorides[2] is used alternately with blood under constant conditions, the solution fails to sustain contractions, while the blood succeeds. The following experiment is an example.

April 10, 1897. A cat's heart was prepared in the usual way, with the cannula in the right ventricle. Ringer's solution at 35° C. was now introduced instead of blood. A slow beating of the right ventricle began: during the first five minutes, 30 beats; during the second five minutes, 6 beats. The contractions were at first strong, but gradually became irregular in force, and spasmodic; they finally stopped. During a third five minutes there were no beats. The solution was now replaced by blood. The beating returned: during the first five minutes, 44 beats; during the second five minutes, 174 beats (60 during the last minute). The contractions were strong and regular throughout fifteen minutes; and later, when the blood was removed and the ventricle washed out, were still seen.

An immediate repetition of the above procedure was followed with similar results; Ringer's solution failed to sustain contractions, while blood caused long-continued beating.

There can remain, then, no doubt of the genuinely nutritive character of the phenomena observed under this method; for the blood enters the ventricle as arterial blood and emerges into the veins of a dark venous color, while rhythmic beats are maintained for a much longer period than can be accounted for on other grounds. Since all other possible channels have been cut off, the veins, which fill with blood, can communicate with the ventricle only by means of the vessels of Thebesius. The coronary arteries can take no part in the circulation, since they are found empty.

One of the conspicuous features in the experiments of Magrath and Kennedy was the fact that an exceedingly small blood-supply was sufficient to maintain the unloaded heart of the cat in regular contractions. These authors published a graphic record of excellent beats which were sustained by a coronary circulation of about 3.3 c.c. per minute, and report a case of fair contractions observed under a circulation of less than 2 c.c. per minute; the customary volume

[1] Hyde (I. H.): Proceedings of the American Physiological Society, Science, Jan. 22, 1897. The paper will be published in full in this Journal, 1898, vol. i.

[2] Modified for mammalian tissues: NaCl, 0.9%; $CaCl_2$, 0.02%; KCl, 0.01%; water distilled in glass. The formula was kindly furnished by Mr. F. S. Locke.

employed ranged from 3.5 c.c. to 13 c.c. per minute. My own results serve to emphasize this fact still further. In supplying the heart with blood through the vessels of Thebesius the circulation was at all times very small — in many cases, even, hardly measurable. In the experiment of April 1, there can have been scarcely more than a mere oozing of blood in and out between the coronary veins and the ventricular cavity through the vessels of Thebesius.

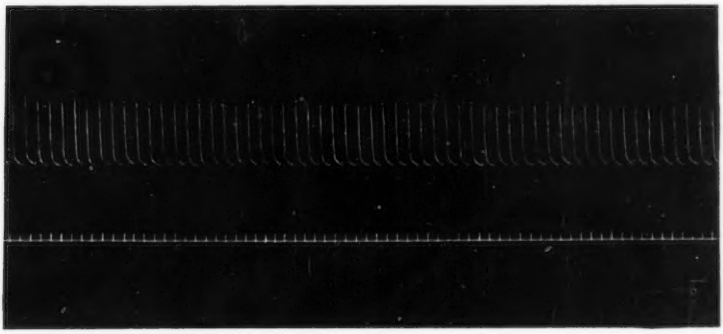

FIGURE 3. From a cat's heart fed from the interior of the right ventricle, April 1, 1897. Recorded one hour after removal of the heart from the body. The upper curve was drawn by means of a Marey tambour connected with the cannula in the right ventricle. The lower curve gives the time in seconds.

The discussion of the nutrition of the heart through the vessels of Thebesius leads now to the consideration of a somewhat striking analogy. It is known that the heart of the frog receives almost its entire nutriment through the branching passages that carry the blood from the interior of the heart nearly to the pericardial surface. My experiments have shown that the heart of the cat may be nourished in much the same way; there is, indeed, a marked resemblance in both method and results between my experiments and many which have heretofore been performed on the heart of the frog. The simplicity of this method of nutrition, as well as its value in bringing the mammalian and batrachian hearts in a physiological sense closer together, seems to assure its further usefulness in experimental work.

III. The Nutrition of the Heart through the Coronary Veins.

The possibility of a nutrition through a back-flow from the auricle into the coronary veins was first suggested by an experiment per-

formed April 5, in which the right ventricle was prepared in the usual way, except that the ligature encircling the heart was omitted. The cannula was tied into the pulmonary artery. Blood was thus allowed to enter the right auricle through insufficiency of the tricuspid valve. The heart was sustained in rhythmic contractions for eight hours, — a period considerably in excess of that observed in nutrition through the vessels of Thebesius alone. It was inferred that

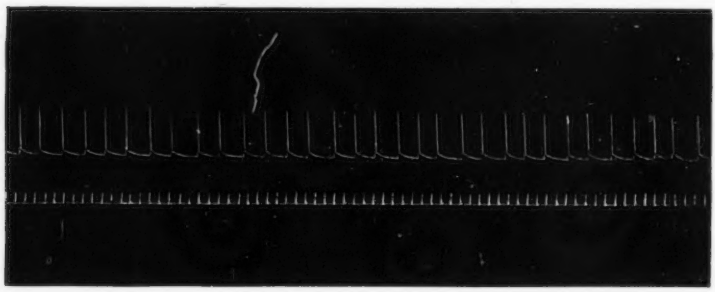

FIGURE 4. From a cat's heart fed from the right ventricle and auricle, April 5, 1897. Recorded six hours after the removal from the body and the beginning of contractions. The upper curve was drawn by means of a Marey tambour connected with the cannula in the pulmonary artery. The lower curve gives the time in seconds.

blood had gained access from the auricle to the coronary veins, and had thus aided materially in the nutrition. The question was therefore submitted to experiment, as follows: —

June 26, 1897. The coronary sinus of a freshly extirpated cat's heart was opened at its middle, and a cannula tied into the distal end. This cannula was supported vertically, and filled to a height of 12 cm. with defibrinated arterial blood. A few minutes after the introduction of the blood both ventricles began to beat. The contractions were coördinated, regular, and complete, and took place at intermittent periods for an hour and a half; they were facilitated by frequent renewals of the blood. The amount of blood contained in the cannula was never more than 4 c.c. During the experiment numerous recoveries from fibrillary contractions were observed, and records secured during the process of recovery. (Fig. 5.)

The above experiment makes evident the fact that under very low blood-pressure the unloaded heart may be made to beat for a long time by feeding it through the coronary veins alone.

IV. The Importance of Nutrition through the Vessels of Thebesius and the Coronary Veins in Certain Pathological States of the Heart.

There are three pathological states upon which the modes of nutrition under discussion appear to have an important bearing; namely, fibrillary contractions, arrest of the heart without fibrillation, and arterio-sclerosis of the coronary arteries.

The recovery of the cat's heart from fibrillary contractions has already been mentioned in the description of my experiments of April 1 and June 26. In one of these the heart was fed from the

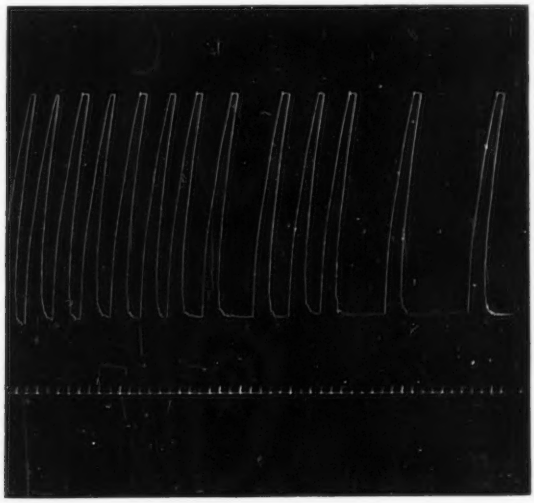

Figure 5. Curve drawn immediately after marked fibrillary contractions, by an ordinary muscle lever attached to the apex of a cat's heart fed through the coronary sinus, June 26, 1897. The fibrillation took place one hour after excision of the heart, and lasted two minutes. The lower curve marks the time in seconds.

ventricle through the vessels of Thebesius; in the other, from the coronary sinus through the coronary veins. It is probable that nutrition through these channels is of great value to the struggling heart, both in preventing fibrillation, and possibly in recovering the heart after fibrillation has set in. That such a recovery may occur, even in the dog, has recently been demonstrated by MacWilliam[1]

[1] MacWilliam: Journ. of Physiology, 1887, viii, p. 299.

and Porter.[1] There is therefore no ground for denying the possibility of recovery in the human heart, although it is likely enough that such instances are extraordinarily rare; and if the cat's heart can be recovered by feeding through the vessels of Thebesius or the coronary veins, the importance of these modes of cardiac nutrition in the fibrillar contractions of the hearts of other mammals can hardly be gainsaid.

It should be remarked that the heart in the living animal is, during fibrillation, in a state particularly favorable to nutrition through both the vessels of Thebesius and the coronary veins. Measurements taken in the left ventricle show that the intracardiac pressure rises as fibrillation draws near,[2] so that the heart is greatly distended even before it has ceased to beat. The arrest of the ventricle lowers the blood-pressure in the aorta, and hence the blood-pressure in the smallest peripheral coronary arteries, to almost nothing. Consequently the passage of the blood through the vessels of Thebesius and the regurgitation from the auricle through the coronary veins are doubly aided; on the one hand by the relatively high pressure in the ventricle and auricle, and on the other by the diminished resistance in the coronary vessels. I have already demonstrated how slight a pressure will drive the blood from the interior of the ventricle or auricle through the cardiac walls. The intracardiac pressure at the onset and in the earlier moments of fibrillation would seem to be more than sufficient to establish such a circulation, giving the quivering organ one chance of recovery, although a desperate chance at best.

In simple arrest of the heart without fibrillation the nutrition through the vessels of Thebesius and the coronary veins may work to great advantage. Here once more the heart is distended; here again the pressure in the coronary arteries has fallen very low: but no fibrillation dissipates the energy of the cardiac muscle in futile, uncoördinated contractions. The occasional recovery of these arrested hearts can scarcely be explained by the theory that leaves the heart un-nourished save through the coronary arteries. It is the pressure in the aorta that drives the blood in the coronary arteries into the cardiac walls in spite of the peripheral resistance. The aortic pressure is maintained by the beat of the ventricle; the loss of a few successive beats lowers it enormously: the reservoir receives

[1] PORTER: This Journal, 1898, i, p. 71.

[2] PORTER: Journ. of Physiol., 1894, xv, p. 133.

nothing, and is speedily drained through the smaller arteries into the capillaries and veins. The coronary capillaries receive their portion with the rest; but whence shall they get more? The pressure in the aorta has fallen, but the peripheral resistance in the coronary system still remains. The power that drove the blood through this resistance is gone, and the capillary areas once fed through the coronary arteries are thereby closed; they can be opened only by the forcible contraction of the left ventricle. But the ventricle lies passive; and should remain so, according to the prevailing belief that the heart is self-nourished and must beat or starve. It is here that the nutrition through the vessels of Thebesius and the coronary veins becomes of importance. The heart *is* self-nourished, but not through its arteries alone; the prostrate ventricle, although it has ceased to feed itself through the coronary arteries, can still be fed by the blood that distends its cavities, and by this endocardiac nutrition may gather strength to resume its load.

Still more interesting is the relation of endocardiac nutrition to arterio-sclerosis of the coronary arteries. The pathologist often finds the coronary arteries thick and stiff with calcareous deposits, their lumen greatly reduced or even wholly gone. And when he looks for the infarcts that should have followed the blocking of the terminal artery, he sometimes sees none. The area formerly supplied by the closed artery is occasionally apparently healthy. Life has continued for months or even years with what seems an impossible heart. No wonder that many anatomists and physicians still contend in the face of conclusive experiments that the coronary arteries are not truly "terminal." How else can such immunity from infarction be explained? What but a collateral circulation through branches freely communicating with other coronary arteries could have kept the ever active muscle from decay? The failure of the distal end of a severed coronary artery to bleed in the profuse way that indicates a free communication with other vascular areas; the fact that infarcts frequently, though not invariably, follow the embolism or thrombosis of these vessels during life; and, most conclusive of all, the easy production of infarcts by the ligation of coronary arteries,[1] — have not convinced some minds. They cling to the occasional freedom from infarction after thrombosis or embolism, and not seldom attempt to strengthen their position by

[1] Kolster: Skandinav. Arch. f. Physiol., 1893, iv, p. 1; also Porter, Arch. f. d. ges. Physiol., 1893, lv, p. 366.

pointing to the fact that one coronary artery can be injected from another.

These writers forget what a terminal artery really is. They forget that terminal arteries, like all other blood-vessels, communicate with their neighbors by capillaries. An artery is terminal, not because it has no communication with neighboring arteries, but because this communication is of a particular kind. "Terminal" means simply that the resistance in the anastomosing branches is greater than the blood-pressure in the arteries leading to these branches. It is this resistance which makes the artery terminal. The concept is physiological, and only secondarily anatomical. The fact that an artery can be injected post-mortem from another artery is no evidence that the living blood in the living organ follows the course of the post-mortem injection. The natural relation between the blood-pressure in the arterioles and the resistance in the communicating vessels cannot be imitated with accuracy. Only injections that pass with great ease can be used as presumptive evidence against the terminal nature of the artery; and, as a fact, aside from rare abnormal cases, injections pass from one coronary artery to another with difficulty or not at all. The advocates of the free anastomosis of the coronary arteries have indeed a difficult position. They must explain how infarcts can follow the closure of freely anastomosing vessels. We who believe in the terminal nature of these arteries need only explain why the closure occasionally fails to produce infarction. And this explanation can now be given.

A certain small number of the cases in which closure fails to produce infarction must be ascribed to the abnormal anastomoses that are occasionally present. It is possible also that the very gradual closure of an artery might permit the gradual dilatation of the communicating vessels until the resistance in them is low enough to divert a part of the blood in the neighboring areas into the anæmic district, and thus gradually establish sufficient collateral circulation to keep the part alive. These possibilities have long been recognized.

A new and effective mechanism for the rescue of the cardiac muscle from threatened infarction is found in the nutrition through the vessels of Thebesius and the coronary veins. Through these ever present channels blood can be drawn to the anæmic area for the occasional saving of hearts in which the blocking has been sufficiently slow. Usually, however, the blood must find the resist-

ance in the arterial capillaries too great to be overcome, and will fail to prevent infarction.

It is evident that the nutrition through the vessels of Thebesius and the coronary veins must modify in no slight degree the existing views of the nutrition of the mammalian heart, and of the manner in which infarction of the heart takes place.

This work was undertaken at the suggestion of Dr. W. T. Porter. I wish, in concluding, to express my grateful appreciation of his encouragement and aid.

Summary.

(1) The vessels of Thebesius open from the ventricles and auricles into a system of fine branches that communicate with the coronary arteries and veins by means of capillaries, and with the veins — but not with the arteries — by passages of somewhat larger size.

(2) These vessels are capable of bringing from the ventricular cavities to the heart-muscle sufficient nutriment to maintain long-continued, rhythmic contractions.

(3) The heart may also be effectively nourished by means of a flow of blood from the auricle back into the coronary sinus and veins.

(4) Nutrition through the vessels of Thebesius and the coronary veins contributes to the recovery of the heart from fibrillary contractions and from simple arrest without fibrillation, and affords a reasonable explanation of many cases in which the cardiac tissues have survived for months or even years the closure of terminal arteries long believed to be their sole supply.

ON THE RELATION BETWEEN THE EXTERNAL STIMULUS APPLIED TO A NERVE AND THE RESULTING NERVE IMPULSE AS MEASURED BY THE ACTION CURRENT.

By C. W. GREENE.

Instructor in Physiology, Stanford University.

[*From the Physiological Laboratory of the Johns Hopkins University.*]

THE experiments described in this paper were undertaken with the idea of ascertaining the quantitative relation between the strength of the external stimulus applied to the nerve, and the strength of the resulting nerve impulse. The nature of the nerve impulse is as yet undetermined. We may recognize its presence in the nerve, however, in two ways: by the change in the electrical condition of the nerve fibres which accompanies the nerve impulse, or by the changes produced in the peripheral organ in connection with the nerve. In the latter case the quantitative changes in the peripheral organ obey laws peculiar to the organ itself, and cannot, therefore, be used directly as an index to the quantitative changes in the nerve fibres.

On the other hand, the changes in the electrical condition of the nerve are immediately associated with and are presumably the direct result of the changes constituting the nerve impulse. The intensity of the electrical change is measurable in the form of the action current. In the experiments described in this paper the action current is taken throughout as a measure of the intensity of the nerve impulse, it being assumed, in accordance with recent authors,[1] that the action current varies proportionately with the change constituting the nerve impulse.

In support of this assumption we may refer especially to the work of Waller, who has made extensive use of the action current in the study of the reactions of nerve fibres to anæsthetics and to many of

[1] A. D. WALLER: Brain, xviii and xix: and Journal of physiology, xviii, p. xxxviii.

BIEDERMANN: Electrophysiologie, p. 658, E. STEINACH: Pflüger's Archiv., 1894, lv. p. 487.

the chemical reagents used in experimental physiology and in medicine. His work offers strong presumptive evidence in favor of the view that there is a direct relation between the action current and the nerve impulse.

Waller also made observations on the relation between the strength of the external stimulus and the resulting electrical change in the nerve. He reached conclusions which will be discussed later in the paper.

Methods and Apparatus.

Determinations of the quantitative relation between the strength of the external stimulus applied to a nerve and the strength of the resulting nerve impulse were made on isolated nerves from the frog (Rana virescens), the terrapin (Pseudemys, two species), the cat, and the dog. The particular nerves used were the sciatic, ulnar, and vagus.

Isolated pieces of nerve five to six centimetres in length were used for experimentation. During an experiment the nerve was laid across two pairs of nonpolarizable electrodes in a moist chamber, one pair of the electrodes being used to stimulate one end of the nerve, the other pair to lead off the action current from the other end of the nerve to a very sensitive aperiodic galvanometer.

The form of stimulus used throughout the experiment was the induced current produced by a du Bois-Reymond induction coil. The secondary circuit included an automatic short-circuiting key, the stimulating electrodes, and an electrodynamometer. The short-circuiting key consisted of a small clock placed horizontally and carrying on its second-hand a platinum connector which revolved in two parallel circular mercury troughs. One of these troughs was interrupted for a definite proportion of its circumference.

The intensity of the stimulus was varied by moving the secondary coil of the induction apparatus toward or away from the primary coil, according to the maker's scale of proportional currents, the intensity of the resulting current being measured by the electrodynamometer in the circuit. The primary circuit was fed by a large storage cell with sufficient resistance in the circuit to give a current of the desired intensity. This arrangement gave a practically constant current during the time limits of an experiment. The current was interrupted by the Neef's hammer attached to the induction coil. Helmholtz's modification was used for equalizing the make and the break inductions.

The electrical measuring instruments used in these experiments are new and especially adapted to physiological work. They may, therefore, be given special mention. Both instruments were devised by Professor H. A. Rowland of the Johns Hopkins University.

The galvanometer is of the d'Arsonval type. It consists of a small coil of fine wire suspended between the closely approximated poles of a powerful horse-shoe magnet. The coil is suspended by a phosphor-bronze filament and the circuit is completed by a spiral spring of the same material at the bottom of the coil. The instrument is rendered aperiodic by a mica vane attached to the suspended coil and swinging in an enclosed box. The deflections of this movable coil are determined by means of a telescope reading the divisions of a scale reflected from a mirror attached to the coil. The reading telescope is attached to the instrument by means of a horizontal arm which can be raised or lowered.

The galvanometer is independent of the earth's magnetism and can therefore be placed upon any convenient supporting surface without reference to the magnetic meridian. When the instrument is once adjusted it is always ready for immediate use, and its sensitiveness, the ease and accuracy with which its deflections may be read, and its freedom from vibrations, make it very convenient in physiological experimentation.

The particular instrument used in these experiments has a resistance of 671 ohms, and gives a current value of 49 ten-millionths of a milli-ampere (49×10^{-10} amperes) per millimetre of scale deflection.

The electrodynamometer consists of a small high resistance coil of fine wire suspended within and at right angles to a fixed coil of high resistance. The free coil is suspended in precisely the same manner as in the galvanometer just described. The instrument is rendered aperiodic by a mica vane, and the deflections are read by means of a telescope and scale, as in the galvanometer. The magnetic field in this instrument is produced by passing the current to be measured through the fixed coil. A current sent through both coils gives a deflection in a constant direction, whether the current be direct or rapidly reversed. It is therefore especially adapted to the measurement of alternating induction currents, such as are used in physiological experiments.

The deflection of the suspended coil in this instrument represents the mean squares of the series of waves of induced current, hence the mean current varies directly as the square root of the deflection.

The resistance of the electrodynamometer used is 3371 ohms. Measured by direct current methods it gives a standard value of 158 ten-thousandths of a milli-ampere (158×10^{-7} amperes) for the unit obtained by taking the square root of the scale deflection measured in millimetres. It must be remembered, however, that this value represents only the mean value of the series of waves of induced current as stated above.

To those accustomed to use induction currents for physiological stimulation, it will be of additional value to know that 2.5 units of current as measured on this electrodynamometer can just be detected by the sensory effect on the tip of the tongue, that 6 to 8 units become sharp, and 12 units painful.

The range of stimulation strength ordinarily used in the laboratory varies between 5 and 10 units of current as defined above. The range of the dynamometer extends from 0.5 to 15 units. This range just about covers the working range of stimulating currents, though scarcely delicate enough to measure minimal stimuli for very sensitive nerves, such as those of winter frogs.

In each experiment the nerve was stimulated for 12 seconds, once every minute, until the desired variation of strength of stimulation was obtained. The resulting action currents were led from the nerve to the galvanometer for measurement. The time of the stimulation was regulated by the automatic short-circuiting clock key already described. The strength of the stimulus was varied by moving the secondary coil toward or away from the primary in the interval between stimulations.

In some control experiments records of the muscular contractions were also taken. In these experiments the gastrocnemius muscle was left in connection with the sciatic nerve and arranged in the usual way in the moist chamber, the muscle lever recording on a slowly moving drum. The sciatic nerve was stimulated near the muscle and the resulting action current was led off from the central end of the nerve to the galvanometer. Experiments of this kind were made on preparations from the frog and the turtle, but not on the nerves from mammals. However, in most experiments the isolated nerve alone was used.

The Results of Experiments.

The quantitative relation between the strength of the external stimulus applied to the nerve and the strength of the action current

produced by it, is shown in the curves constructed from the experiments. In these curves I have plotted units of increase of stimulating current along the abscissæ and the associated change in the strength of the action current along the ordinates.

One millimetre of scale deflection of the galvanometer by the action current has a value of 49 ten-millionths of a milli-ampere, as previously stated. There is a great difference in the absolute values of the action currents obtained from different nerves, but as we are concerned here only with the relative variations in values I have reduced all curves to a uniform magnification in order to facilitate comparisons.

Nerves of the Frog. — The plotted curve expressing the relation between stimuli of different strengths applied to a frog nerve and the strengths of the resulting action currents shows three characteristic parts (Fig. I.): (1) an abruptly ascending straight limb, including the range from minimal nerve stimuli to stimuli above the strength that calls forth maximal muscular contractions; (2) a middle portion, in which the curve is still ascending but strongly concave to the abscissa; (3) a supra-maximal straight portion parallel to or more often slightly diverging from the abscissa.

These regions I shall now describe in greater detail. The first record of a current of action in a frog nerve was obtained when the nerve was stimulated with an induced current just strong enough to produce a minimal muscular contraction. This was the usual result in test experiments, although sometimes the minimal muscular contraction was obtained with a stimulus slightly weaker than that causing a readable action current in the nerve. In every case the minimal action current produced in the galvanometer a deflection of only a fraction of a millimetre.

A series of stimuli applied to the nerve, increasing above the minimal stimulus by very small but equal increments up to a strength about twice that necessary to call forth a maximal muscular effect, produced a relatively strong and rapid increase in the action current. This increase in the action current was by increments proportional to the increase in stimulus, giving in the plotted curve a straight line. Such slight variations as occurred in successful experiments were apparently within the limits of error of determination. The strength of a minimal stimulating current for the nerve varied from 0.02 to 0.2 units. The increase in stimulus that was necessary in order to call forth maximal muscular contractions in test experiments, was approxi-

mately 0.2 of a unit. The upper limit of the first straight portion of the curve is not sharply bounded.

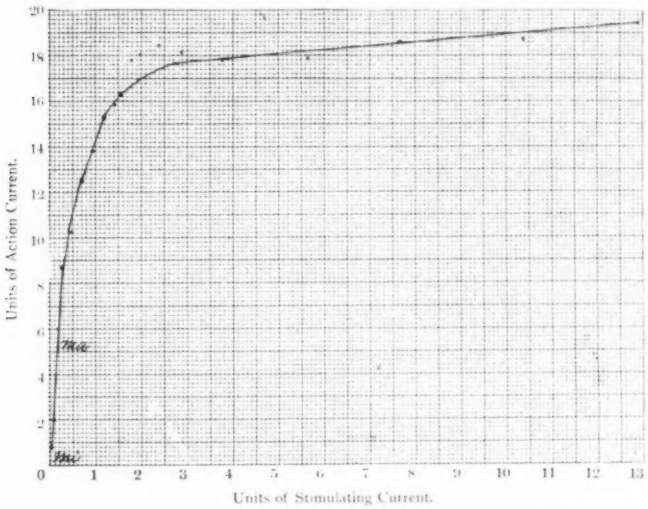

FIG. 1. SCIATIC OF THE FROG. EXPERIMENT 39.

Curve representing the quantitative relation between the strength of an external stimulus applied to the frog's sciatic and the strength of the resulting action current. The abscissæ represent units of stimulating current (1 unit = 15.8×10^{-7} amperes). The ordinates represent units of action current (1 unit = 49×10^{-10} amperes). The dots on the plot represent the individual readings. The mean for this series of readings was drawn after a comparison of several typical experiments.

Mi. Minimal muscular effects. Ma. Maximal muscular effects.

A further increase in the strength of the stimulus above that just described produced an increase in the action current of the nerve, but the added increments of action current accompanying the increase in stimulus were successively smaller. At this point the plotted curve is strongly concave to the abscissa. This middle portion of the curve of relation between the strength of the stimulus and the strength of the action current varies in extent and in degree of concavity, and its limits can be determined only very roughly.

A further increase in the strength of the stimulus produced only a slight additional increase of the action current, even though the strength of the stimulus was increased tenfold and more. This slight

increase in the action current was by increments proportional to the increase in stimulus. When plotted, the results give a straight line slightly diverging from the abscissa. Occasionally there is no increase in the amount of the action current, and the line is then parallel to the abscissa.

The nerves of winter frogs are sometimes very irritable and the relations of minimal stimuli to the corresponding action currents are accordingly difficult to determine. The strength of minimal stimuli for many frog nerves was too slight to be measured by the electrodynamometer, and in such experiments it was determined indirectly by the corrected scale of the induction coil.[1] In these very irritable nerves the abruptness in the increase in action current with small increase above minimal stimuli is most marked. Variations and irregularities were frequently obtained also in the response of frog nerves to stronger stimuli.

Nerves of the Terrapin. — Nerves of the terrapin (Pseudemys), are much less irritable than those of the frog, but the curve of relation between stimulus and action current response, plotted from experiments on the sciatic of the terrapin, exhibits the general characters just described for that of the sciatic of the frog. That is, it shows a beginning straight limb of rapidly increasing action current produced by slight increase in the energy of the stimulus, a middle portion concave to the abscissa in which the action current still increases, but by diminishing increments, and a long supra-maximal straight limb slightly diverging from the abscissa.

The first straight part of the curve usually ascends less abruptly from the abscissa and the second curved portion is usually longer and less concave than in the curve from the frog's sciatic. The series of tests as a whole was more regular and constant than in the experiments on the frog's sciatic.

The total action current obtained from the nerves of the terrapin was relatively much less than that obtained from the frog's sciatic. A minimal stimulus for the sciatic of the terrapin varied from 0.7 to 2 units of stimulus; an increase above this by 0.3 to 0.7 units produced a maximal stimulus for the muscle attached to the nerve in test experiments.

[1] By a new arrangement of the dynamometer, suggested by Professor Rowland, this difficulty has been obviated, the sensitiveness of the dynamometer being so greatly increased that minimal or sub-minimal stimulating currents, even for very irritable nerves, can probably be determined without difficulty.

The results of experiments on the vagus of the terrapin have been quite variable. In eight experiments no action current was obtained from the vagus, even with excessively strong stimuli. In other experiments, especially after the nerves were kept in the moist chamber for from one to three hours, an action current of relatively slight intensity was obtained. The results of experiments which yielded the most pronounced action currents, when plotted, exhibit in a degree the relations shown by the curve from the sciatic of the terrapin. However, the first straight portion of the curve is obscure in experiments on the vagus in that it merges at once into the second or strongly concave portion. The upper straight limb of the curve is quite closely comparable to that in curves from the sciatic nerve.

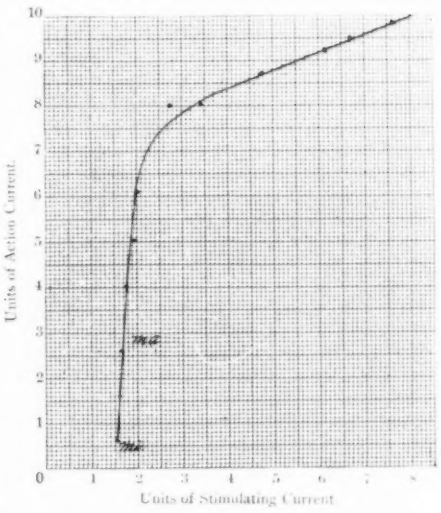

FIG. 2. SCIATIC OF THE TERRAPIN. EXPERIMENT 102.

Curve representing the quantitative relation between the strength of an external stimulating current applied to the sciatic of the terrapin and the strength of the resulting action current. As in Fig. 1, the abscissæ represent units of stimulating current, while the ordinates represent units of action current. The upper limb of the curve in this experiment diverges from the abscissa more than does the average of the whole set of experiments.

Mi. Minimal muscular effects. Ma. Maximal muscular effects.

The striking difference in irritability of nerves from the frog and from the terrapin is shown by Figs. 1 and 2.

Nerves of the Cat and the Dog. — Nerves of the cat and the dog were used under precisely the same conditions as those of the frog and the terrapin. The curve expressing the relation between the strength of the external stimulus and the strength of the action current in nerves of the cat and the dog (Figs. 3 and 4) is very like that obtained from the frog or the terrapin. Beginning with minimal stimuli applied to the nerve and increasing by small but equal increments of stimulation there is a rapid increase in the amount of the action current also by equal proportional increments.

This ascending straight limb of the curve is followed by a middle portion increasing by diminishing increments and thus concave to the abscissa, and this, finally, by a long supra-maximal straight portion diverging slightly from the abscissa. The middle portion of the curve is usually longer and less concave (Fig. 4, *ab*) than in the curves from the nerves of the frog or the terrapin, but sometimes this difference is not apparent. In a small percentage of experiments on the sciatic of the dog I have obtained an initial short curve convex to the abscissa. That is, with an increase by equal increments above a minimal stimulus for the nerve there is for one or two readings an increase in the action current by successively increasing increments. This short initial part of the curve is always followed by the first straight portion as described above. It should be stated here that the long and tedious precautions for cooling the animal to room temperature before its death, as described by Bernard, Schiff, and Israel,[1] seemed unnecessary and were not observed. The animals used were such as had been killed in the laboratory at the end of other experiments. The nerves were taken soon after the animal was killed in some instances, and in others not until the animal had cooled to near the room temperature. In one case, one sciatic of a dog was removed at once after the animal was killed, the other after it had cooled to near the room temperature. No difference was observed between the character of the results in experiments made on the two nerves immediately thereafter. However, after being kept over night on clean filter paper moistened with physiological saline solution, the

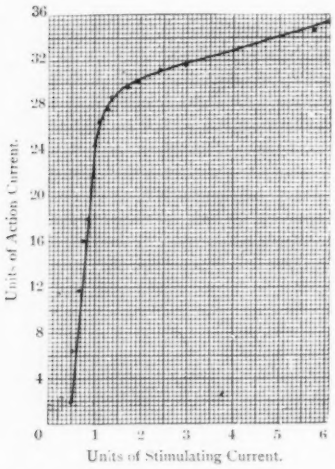

FIG. 3. ISOLATED SCIATIC OF THE DOG. EXPERIMENT 106.

Showing the relation between the strength of an external stimulus and the strength of the resulting action current. Units of stimulating current along the abscissæ, units of action current along the ordinates.

For the full extent of the upper straight limb of the curve, compare with Fig. 4. This experiment was performed after the nerve had been kept alive in the moist chamber at room temperature for 16 hours.

[1] OSCAR ISRAEL: Arch. für Anat. u. Physiol. (physiol. Abth.), 1877, p. 443.

warm nerve gave no response even to the strongest stimuli, while the cooled nerve was still alive as shown by the strong action current. A nerve taken from the body of a dog after 15 hours, was dead, while nerves from the same dog removed immediately and kept on filter paper for 15 hours were still alive and very irritable, as shown by the marked action current caused by stimulation.

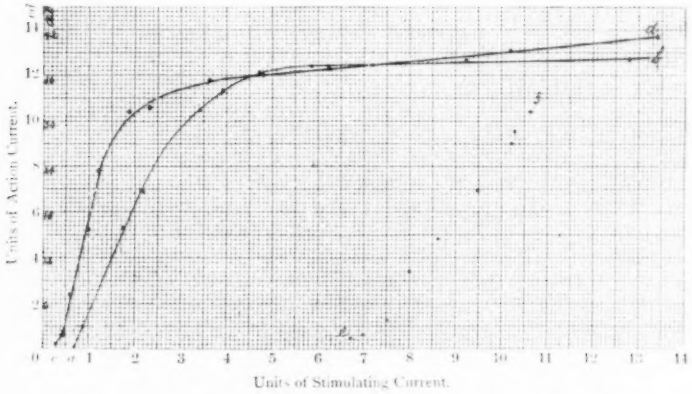

FIG. 4. SCIATIC OF THE DOG. EXPERIMENTS 91, 95, AND 118.

Curves expressing the relation between the strength of stimulating current and the resulting action current. No. 91, *ab*, from the nerve immediately after its removal from the body. No. 95, *cd*, from the same nerve after 17 hours in a moist chamber at room temperature. The curve *cd* shows in comparison with the curve *ab* the increase in irritability and decrease in the amount of the action current which occurs when nerves are kept for some time. No. 118, *ef*, the beginning of a curve introduced here to show the initial minimal portion convex to the abscissa. Curve *ef* also shows the phenomenon. The values of the stimulating current and the action current are not given in curve *ef*, but the magnification is about twice that of the curves *ab* and *cd*.

Nerves from dogs and cats remain alive in the moist chamber at room temperature a surprisingly long time. Nerves from the dog have been frequently kept alive over night and experimented on the next day 15 to 20 hours after removal from the body of the animal. In one case two sciatics and an ulnar of the dog were alive and hyperirritable after 25 hours, and the following morning, after an isolation of 41 hours[1] at room temperature, the ulnar still gave a small action current; the two sciatics gave no action current, *i. e.*, were no longer

[1] L. Fredericq obtained an action current after 24 hours. Archiv. f. Anat. u. Physiol., 1880, p. 70.

capable of responding to stimuli. Even in these sciatics, however, very strong currents of rest were present.

I have uniformly obtained a strong action current from isolated nerves of the dog. The action current decreases after 12 hours (see Table), but a current may still be obtained after at least 41 hours. The action current varied from 20 to 30 per cent of the demarcation current in fresh nerves. The strongest action current Grützner[1] obtained from rabbit nerves did not exceed 4 per cent of the demarcation current. As the nerves were kept, the demarcation current increased for some time, becoming two to three times the original value after 15 hours, — the measurement being made after a fresh section of the nerve. This increase in the value of the demarcation current was true also for the nerves of the terrapin, and has been described before in the nerves of frogs.[2]

TABLE

Showing data from successive experiments on the same nerve, to illustrate the increase in irritability and the decrease in maximal action current, which occur when the nerve is kept alive on filter paper wet with physiological saline solution.

From the Ulnar Nerve of the Dog.

Ulnar of Dog.	Strength of Stimulating Current giving rise to a minimal action current.	Strength of Action Current with a supra-maximal stimulus, 10 units.
After 20 minutes.	1.94 units.	33.2 mm. of deflection.
" 18 hours.	.54 "	17.4 " "
" 24 "	.25 "	9.8 " "
" 41 "	.55 "	0.9 " "

The irritability of isolated nerves from the cat and the dog increased for several hours, 24 hours at least, and then decreased until its final disappearance. The test on which this statement is based is the strength of a minimal stimulus necessary to produce an action current in the nerve.

Comparison of Results.

From about one hundred and twenty experiments I am unable to deduce any general law applicable to the entire curve of relation

[1] Grützner: Pflüger's Archiv., 1881, xxv, p. 278.

[2] Howell: Journal of physiology, 1894, xvi, p. 476.

between the external stimulus applied to a nerve and the strength of the action current produced. There is a close similarity in the form of the curves expressing the results of experiments on nerves from the three classes of animals used. In every case the entire curve shows three distinct parts as described above. Each of these parts varies according to its own laws. The first part and the last portion vary according to arithmetical ratios, but the ratios are different in the two portions.

Waller,[1] from his experiments, describes the relation of the strength of the external stimulus and the action current response as an *S*-shaped curve consisting of three portions: (1) an initial "short submininimal portion convex to the abscissa, increasing by increasing increments; (2) a long straight middle portion, inclusive of and beyond the functional range of nerve measured by maximal muscular effects, increasing by equal increments; (3) an ultra-maximal portion far above the values of maximal functional effects concave to the abscissa, increasing by diminishing increments."

The first sub-minimal portion of the curve that he describes I have been unable to obtain on the nerves of the frog. But on the sciatic of the dog I have obtained a short initial curve similar to that described by Waller for the nerves of the frog, although I cannot say what relation it bears to minimal muscular contractions. This initial curve in the nerves of the dog, when present, is much more strongly marked than in the single curve which Waller shows. In fact, the particular experiment that he has plotted exhibits a variation scarcely greater than might be accounted for by the limits of error in determination. However, some of his tables,[2] if plotted, show the phenomenon much more strongly, while others do not exhibit it at all.

My results on all nerves confirm Waller's statements with reference to the second part of the curve which he describes. That is, I have found that variations in the strength of the stimulus between the limits of strength that call forth minimal and maximal muscular contractions are accompanied by proportionately increasing increments of action current. In experiments in which I have used the nerve alone, this region is a straight line in the plotted results. Waller's supra-maximal portion of the curve seems to correspond with the

[1] WALLER: Brain, xviii, p. 200.

[2] WALLER: Journal of physiology, 1895, xviii, p. xxxii, Exps. 103, 130a, 130b.

middle portion of my curves, which, following his description, I have spoken of as concave to the abscissa.

The third or supra-maximal straight portion, which I have described and figured, he does not describe, although the data for it is contained in one of his protocols (No. 106). Throughout this portion of the curve a wide variation in the strength of the stimulating current occasions but little and in some cases practically no variation in the strength of the action current. We have here a phenomenon which at first sight suggests a comparison with the maximal contraction of a muscle. This maximum is reached, in the nerve, at a point far beyond the strength necessary to cause a maximal muscular contraction. It lies, therefore, beyond the probable range of normal functional activity. As between the muscle and the motor nerve, however, it may be said that the latter is capable of imparting a stimulus far in excess of that necessary for the production of a maximal shortening in the muscle. How completely this relation may hold when the nerve fibre is stimulated from its cell instead of directly by artificial means, cannot be determined.

Finally, I wish to express my deep obligation to Professor W. H. Howell, at whose instigation this work was undertaken. To his many helpful directions and suggestions given while prosecuting the investigation, and especially to his kindly criticism during the preparation of the manuscript, are chiefly due whatever of value attaches to this paper.

ON THE NATURE OF THE CARDIOPNEUMATIC MOVEMENTS.

By S. J. MELTZER.

[*From the Department of Physiology of Columbia University, at the College of Physicians and Surgeons, New York.*]

FOR more than thirty years it has been known that the air in the respiratory tract shows slight periodical oscillations, synchronous in rhythm and time with the cardiac beats, — the cardiopneumatic movements, as they have been called since Landois first gave them the name.

C. Voit[1] observed these movements while breathing through a Müller's valve. During a respiratory intermission in which the glottis remained open and the nose closed, regular oscillations were noticed consisting of tiny inspirations and expirations. Voit found the inspiratory motion synchronous with the systole, and the expiratory with the diastole of the heart. He explained the phenomenon by the assumption that each systole — diminishing the volume of the heart — causes a lowering of pressure within the thoracic cavity, and thereby an aspiration of air by the lungs, — an inspiration; while the diastole increases the pressure, and causes an expiration.

Two years later Terné van der Heul,[2] under the direction of Donders, attempted to get tracings of these movements as they are obtainable from the nose, and was surprised to find that, in his case, the inspiration coincided with the diastole and the expiration with the systole, the tracing presenting a regular sphygmogram. It is probable, however, that in van der Heul's case the glottis was closed while the tracings were taken, these therefore being in fact nothing but sphygmograms, *i. e.*, the variation in the volume of blood within the closed cavity of the nose. Many persons, as Mosso has shown, are indeed unable to keep the glottis open while they stop breathing. The writer of this article can witness to that fact. In the few attempts which he has made to obtain cardiopneumograms from the nose the result has been invariably a sphygmogram.

[1] VOIT: Zeitschrift für Biologie, 1865, i. p. 390. The phenomenon had already been described before Voit by Buisson, Gaz. med. de Paris, 1861, p. 320.

[2] TERNÉ VAN DER HEUL: Nederlandsch Archief voor Genees- en Natuur-Kunde, 1867.

Ceradini[1] studied the movements at first by means of a manometer connected with the nose or mouth, and containing smoke or colored liquid; he confirmed the statement of Voit, and also adopted his explanation of the phenomenon. In a later study,[2] however, Ceradini modified his first interpretation. He came to the conclusion that the systolic condition of the heart could not change the pressure within the thoracic cavity as long as the blood put out from the left ventricle is still within the cavity. Ceradini, therefore, now assumed that the oscillations did not originate from the change in the volume of the heart, but from the change in the volume of blood present in the thoracic cavity; the inspiration being due to the outflow from the cavity of the chest, and the expiration due to the inflow of blood into the cavity. Ceradini also obtained tracings of these movements by means of an instrument which he called "Hæmothorakographion,"[3] but never published them.

In 1876 Landois[4] published an elaborate monograph on these oscillations, which he termed, as stated above, cardiopneumatic movements. He studied the movements with the aid of the manometric flame, and, also, by means of his cardiopneumograph, obtained tracings of them from the nose and mouth of men and from the trachea of curarized dogs. The skeleton of his tracings shows a sudden steep inspiratory, and a gradual, slanting expiratory undulation, which Landois, adopting Ceradini's later view, explains by the sudden arterial output of blood from, and the gradual venous flow of blood into, the thorax. Besides these main movements, Landois noticed on his tracings little secondary notches and peaks which he attempted to explain by certain subsidiary but constant causes. The rebound of the arterial blood causes a tiny peak on the expiratory line. Landois insists that each inspiratory movement is preceded by a small sharp expiratory motion, which he explains by an assumption that I shall not discuss here. Mosso,[5] on the other hand, who accepts the views of Ceradini and Landois with regard to the chief cause of these movements, claims that no short respiratory upstroke precedes the inspiratory movement, and that, in his opinion, the beginning of this latter

[1] CERADINI: Heidelberger Jahrbücher der Literatur, 1869, p. 912.

[2] *Ibid.*: Annali universali di medicina, 1870, p. 587.

[3] This instrument, as well as the cardiopneumograph of Landois, is practically nothing more than a Marey's tambour.

[4] LANDOIS: Graphische Untersuchungen über den Herzschlag. Berlin, 1876.

[5] MOSSO: Die Diagnostik des Pulses, 1879.

movement is caused by the widening of the chest due to the heart impulse.

Finally, Martius, who wrote a very elaborate article on the "cardiopneumatic movements in the œsophagus," should also be mentioned, but I shall not discuss his article here. I wish only to say that Martius, in his very elaborate analysis of his tracings, also adopts the view that the flow of blood into and out of the thorax is the chief cause of the cardiopneumatic undulations.

Thus, the authors mentioned, and many other writers[1] on the cardiopneumatic movements, all agree, so far as I can see, that the movements are expressions of the variations of pressure within the air-tight thoracic cavity caused by changes either in the volume of the heart or in the volume of the blood contained in the thoracic cavity.

A recent article by Haycraft and Edie[2] opposes this view. These authors state that the cardiopneumatic movements "occur equally well with the chest cavity open and freely communicating with the outer air" (p. 429). It is obvious, therefore, they say, that the hypothesis of Ceradini and Landois can hardly be accepted as explaining the cardiopneumatic movements. They offer another hypothesis instead, namely, that the movements are "simply due to the heart pressing against the lungs, and that the lungs acted like an oncometer placed around it" (p. 430). The proof for this hypothesis they see in the fact that the cardiopneumatic movements almost entirely cease on lifting the heart away from the lungs. The writers are so thoroughly convinced of the correctness and simplicity of their position that they can hardly understand why it was overlooked by all the other writers on the subject, especially by Landois, who was the first one to obtain tracings of these movements. "It is a pity that he did not go a step or two further," they say, "their entire explanation must have dawned upon him" (p. 435).

The purpose of this Paper is to test the validity of the views advanced by Haycraft and Edie. Before entering into a further discussion, I wish, however, to remark that identical views were

[1] Loven: Nord. med. Ark., 1870, no. 19: P. Bert: Leçons sur la physiologie comparée de la respiration, Paris, 1870, p. 388: Von Bruns: Berliner klinische Wochenschrift, 1872, p. 130: Regnard: Revue mensuelle de médicine et de chirurgie, 1877, p. 333: Lépine: *ibid.*, p. 394: François-Franck: Travaux du laboratoire de Marey, 1877, p. 233.

[2] Haycraft and Edie: Journal of physiology, 1891, xii, p. 426.

advanced by Klemensiewicz [1] about fourteen years before Haycraft and Edie, just after the appearance of the monograph of Landois. The original article is not accessible to me, but there is a short report of it in the Jahresbericht of Hofmann und Schwalbe [2] which I will quote here in part. "Klemensiewicz reports experiments on the cardiopneumatic movements, which can also be seen in the frog. He rejects the explanation of Landois because the phenomenon is also present when the thorax is open. The movements are due rather to the intimate relation between the heart and the lungs, the latter, like a large Marey's tambour, registering all the movements and vibrations of the heart." We see here the same hypothesis as that of Haycraft and Edie, and also the same argument for rejection of the hypothesis of Landois and others. In discussing the new hypothesis and the arguments against the older one, I shall use the statements of Haycraft and Edie, as I do not know the experiments upon which Klemensiewicz has based his opinion.

According to Haycraft and Edie, the cardiopneumatic curve represents the variations in the pressure exerted by the heart upon the lungs. As the heart slowly changes its size during diastole, it presses upon the lungs and causes the gradual (expiratory) upstroke. In the beginning of the systole the heart at first "resents" its distortion by the lungs, — it "asserts" itself, which again causes a small but steep upstroke; then as it becomes smaller in all dimensions, it recedes from the lungs, which now expand, thus causing a sharp downstroke, — an inspiration. In a certain sense the theory of Haycraft and Edie coincides with the original hypothesis of Voit and Ceradini, inasmuch as both agree that the movements are due to the change of pressure caused by the change in the size of the heart; but while Voit and Ceradini meant the pressure exerted upon all the contents of the thoracic cavity, Haycraft and Edie mean only the direct pressure upon the lungs.

The interpretation of these authors, however, seems to me to be open to some criticism. We can understand why the pressure of the heart upon the lungs during diastole should produce an expiratory movement; we can admit the possibility that the "self-assertion" of

[1] KLEMENSIEWICZ, R.: Beiträge zur Demonstration des Pulses und Herzstosses mittelst der manometrischen Flamme, nebst Versuchen über die sog. cardiopneumatischen Bewegungen. Mitteilungen des Vereins der Aerzte im Steiermark, 1875–76.

[2] Jahresbericht über die Fortschritte der Anatomie und Physiologie, 1877, p. 56.

the heart will also cause a slight expiratory puff; but we cannot comprehend why the recession of the heart during systole should be followed by an inspiratory movement, — by an expansion of the lungs. Even in a state of collapse, the lungs are not perfectly atelectatic, but contain some air, and their elastic tissues are still stretched. When, now, air is driven out by the alleged pressure of the heart, expanding in diastole, what force is then present in the open chest that could distend the lungs anew against their own elastic tension, after they are released from the heart's pressure? In the tracings obtained from the lungs while the thorax is open, the apparent expansion of the lungs after the alleged diastolic pressure of the heart upon them has been withdrawn may be due to the elastic reaction of the rubber cover of Marey's tambour, which strives to return to its position of equilibrium after being stretched by the preceding expiration caused by the hypothetical pressure of the heart in diastole. But in the normal individual, in whom the elastic lungs are always considerably stretched, what could cause the lungs to expand again during systole against the strong pull of their elastic fibres; especially in such experiments as Landois and Ceradini made, in which the cardiopneumatic movements were demonstrated by the gas-flame and by smoke in a manometer? Smoke is lighter even than air, but, nevertheless, an inspiratory movement is seen in the smoke-column during each systole. What force except the negative pressure could compel the lung to follow the receding heart?

Again, Haycraft and Edie explain the entire cardiopneumatic curve also by the pressure of the heart upon the lungs, and do not permit the change in the pressure within the thorax to exert any influence upon it. But it is, nevertheless, an indisputable fact that during each cardiac cycle there is a considerable variation in the volume of blood present in the thorax. Now, why should this change of volume not cause a change of pressure in the normal, air-tight thorax, and why should this change of pressure not cause an expiration and inspiration, and leave a marked impression upon the cardiopneumatic curve? In this connection, it may be observed that Haycraft and Edie were not very fortunate in comparing the effect of the heart upon the lungs with the working of an oncometer. Here, too, the contractions of the organ enclosed within the oncometer are transmitted only by the changes in the negative pressure which they cause in the air-tight capsule of the instrument.

Furthermore, Haycraft and Edie in support of their statement that the open thorax has no influence upon the cardiopneumatic movements have published two figures, each containing two tracings, — one taken before and the other after the opening of the thorax. In both figures, however, the tracings taken when the thorax was open differ distinctly from those taken from the normal animal. I reproduce here one of these figures.

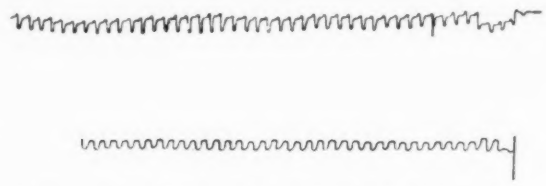

FIG. 1. (Fig. 4 in Haycraft and Edie's article; Journal of Physiology, 1891, xii, p. 431). "Tracing (1) was taken from a rabbit with its chest cavity in normal condition; tracing (2) after making a free opening into the cavity."

In order to gain a personal insight into this problem I have repeated the experiments of Haycraft and Edie. These authors do not tell us directly from what animals they derived their results. There is a remark in their article that they have experimented with the lungs of rabbits and sheep, but this has reference to another kind of experiments. It is said, however, that the tracings which they present were obtained from rabbits. I have therefore first experimented on rabbits. The method was in general the same as that employed by the authors mentioned and by Landois. The animals were given chloral and then curare, and were kept alive by artificial respiration. The tracheal cannula was connected with a Y tube, each limb being provided with a stop-cock. One limb was connected with the apparatus for artificial respiration, and the other with a Marey's tambour registering on a revolving cylinder. When the stop-cock leading to the apparatus for artificial respiration was closed and that leading to the Marey's tambour opened, the cardiopneumatic movements soon appeared. After taking a few tracings from the normal animal, the chest was opened and tracings were again taken. I repeated these experiments on eight rabbits, from every one of which I uniformly obtained the following result: when both pleural cavities were freely opened there was no cardiopneumatic oscillation on the tracing from the trachea.

Fig. 2 shows a part of the tracings taken just before and after the opening of the thorax. The tracing taken soon after both sides of the thorax were opened is simply a straight line, drawn from a lower level on account of the collapsed condition of the lungs.

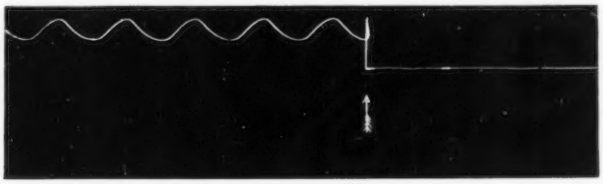

FIG. 2. The upper tracing is a cardiopneumogram from the trachea of a rabbit. On the left of the arrow are the cardiopneumograms taken while the chest was intact. After opening both pleural cavities all movements disappeared, and the tambour registered the straight line to the right of the arrow.

My results then were in direct contradiction to those described by Haycraft and Edie. I soon discovered, however, that there was a difference between the method of opening the thorax employed by Haycraft and Edie and that employed by myself. I usually opened each pleural cavity separately on their respective sides of the sternum. In one experiment in which I removed a part of the sternum some slight undulations could indeed be noticed on the tracing obtained from the trachea immediately after opening the chest (see Fig. 3).

Haycraft and Edie opened the abdominal cavity and cut away the anterior attachments of the diaphragm along with the anterior chest wall in its lower part. Of this method, which Haycraft calls the best,

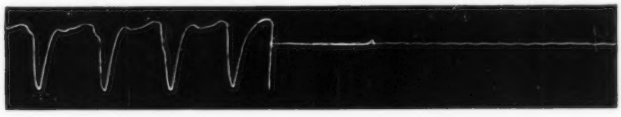

FIG. 3. Cardiopneumatic tracing, from a rabbit. At *x* a part of the sternum was removed; some fine undulations are noticeable on the line to the right.

he himself speaks as follows: "As soon as this is done, the heart will fall down in its natural bed formed posteriorly by the lungs and will be carried up and down by them with the movements of respiration; it will be loosened from its more solid moorings to the chest wall and will be seen floating as it were upon the lungs. It is in this position that physiologists from Harvey's time onwards have chiefly

studied its movements, making, I think, too little allowance for the fact that the organ is in an entirely unnatural condition in respect to its attachment."[1] I think that Haycraft is correct in this, but that he and Edie themselves make too little allowance for the fact that in their experiments the heart was in an entirely unnatural condition with respect to its attachments. I have repeated their experiment also on a number of dogs, and have convinced myself more than once that when the pleural cavities are opened without disturbing the natural relations of the heart to the front wall and diaphragm, the cardiopneumatic movements disappear either entirely or are hardly perceptible. When, however, as in Fig. 3, the attachments to the sternum and the diaphragm are removed and the heart allowed to fall back upon the lungs, some distinct movements appear again.

The experiment illustrated by Fig. 4 shows us (1) that the opening of the thorax, without disturbing the natural attachments of the heart, nearly destroys the movements (see tracings Nos. 2 and 4); (2) that the closure of the opening in the chest, though surely not absolutely air-tight, brings the movements out again to a certain degree (tracings Nos. 3 and 6); (3) that the removal of the normal attachments of the heart causes the heart to fall back upon the lungs and brings out movements that seem to be different in size and character from those which occur when the chest is air-tight and intact (tracing No. 5).

There is still another point which deserves special comment. If the communication between the trachea and the Marey's tambour were established immediately after the artificial respiration is discontinued, the rubber cover of the tambour would be exposed to an abnormally high pressure by the air escaping from the inflated lungs. To avoid this I have regularly permitted the thorough escape of the air from the lungs before a tracing was taken. To attain this I placed a T-tube between the stop-cock on the limb leading to the apparatus for artificial respiration and the tracheal cannula; this tube had a stop-cock on its vertical limb which was kept slightly open during the artificial respiration, and which I might call "the relief stop-cock." Before taking a tracing the following order was observed. First the relief stop-cock was opened fully, then the stop-cock of the artificial respiration was closed and that leading to the tambour was opened; and, finally, after the lever of the tambour reached its nor-

[1] HAYCRAFT, J. B.: The movements of the heart within the chest-cavity and the cardiogram. Journal of physiology, 1891, xii. p. 447.

mal position again, the relief stop-cock was closed and a tracing taken. With these precautions the tambour was under an equal atmospheric pressure inside and outside while registering the movements. If the relief stop-cock was closed before all the surplus air had escaped, the lungs did not thoroughly collapse and the tambour registered some movements, although the thorax was open and the attachments of the heart thoroughly removed; the movements disappeared as

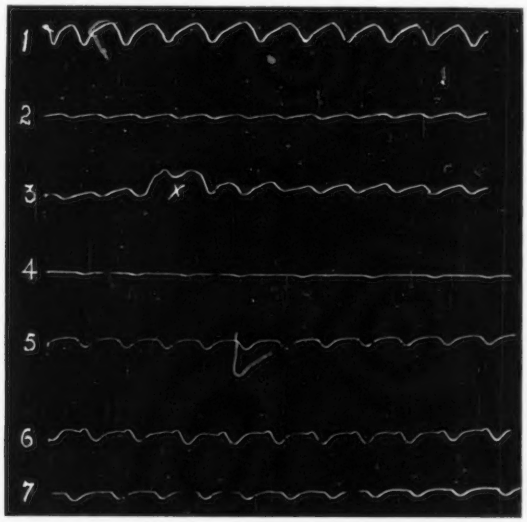

FIG. 4. (1) Shows the cardiopneumatic movements in a small dog with chest unopened. (2) Taken after the left pleural cavity was opened, the undulations becoming very small. (3) The continuation of tracing 2; closing the opening with a towel caused the movements to increase again. (4) Taken after both pleural cavities were opened; there is only a trace of the movements to be noticed. (5) Taken under the same conditions, but after the attachments of the heart to the front wall and the diaphragm had been thoroughly removed. The movements are again considerably increased, but they differ in character from the normal pneumocardiograms of the same dog, and resemble tracing 2 in Fig. 1 (from Haycraft and Edie, see above). (6) Taken under the conditions of tracing 5, but both openings were closed with towels. The size and especially the character is changed. (7) The towels were removed and the tracings are once more the same as in 5.

soon as the air was permitted to escape thoroughly. These movements were quite large at times, especially when the attachments of the heart were thoroughly removed. The tracing in Fig. 5 illustrates this case.

While this tracing was being taken, both pleural cavities of the dog were wide open and the attachments of the heart removed, but the lungs were still considerably inflated and the heart was buried between them. The artificial respiration was interrupted for a long period; the dyspnœa caused a slowing of the beats of the heart, which, becoming quite large during each diastole, pressed the lungs to the sides of the thorax, and hereby caused large but not characteristic cardiopneumograms. Haycraft and Edie, it should be remarked, do not tell us what precautions they have taken to avoid

FIG. 5. Cardiopneumatic curve taken from a large dog. Dyspnœa; thorax wide open; attachments of heart thoroughly removed, but lung still quite inflated.

this artificial condition of affairs. We read there: "On stopping the respiration, opening the communication with the tambour, and clamping the tube passing to the bellows, the cardiopneumatic movements were well seen" (p. 430). I know by experience that even with an opening widely communicating with the air, it takes some time for an artificially ventilated lung to reach the limit of collapse. Haycraft and Edie do not tell us explicitly that they have taken the necessary precautions; perhaps the lungs of their animals still contained surplus air when the tracings were taken, giving them artificial cardiograms not to be obtained under normal conditions.

My experiments justify the following conclusions: —

(1) The cardiopneumatic movements disappear when both pleural cavities are open, provided the heart retains its normal attachments and the lungs are thoroughly collapsed before the tracings from the trachea are taken;

(2) The results of Haycraft and Edie might have been caused by their method of opening the thorax, which permits the falling back of the heart upon the lungs, and also might have been influenced by an incomplete collapse of the lungs;

(3) Without the assistance of the elasticity of the rubber cover of the tambour, the lungs in the open chest cannot follow the receding heart in the systole and no inspiratory movement can occur;

(4) The hypothesis offered by Haycraft and Edie that the lungs act like an "oncometer" placed around the heart cannot be accepted as an explanation of the normal cardiopneumatic movements.

For these reasons I agree with the majority of the writers that the cardiopneumatic movements have their origin in variations of the intrathoracic pressure caused by certain changes in the circulation.

THE FUNCTIONS OF THE EAR AND THE LATERAL LINE IN FISHES.[1]

By FREDERIC S. LEE.

[*From the Physiological Laboratory of Columbia University, at the College of Physicians and Surgeons, New York.*]

ALL vertebrate morphologists are well aware that two of the prominent vexed problems of their science are the history, ontogenetic and phylogenetic, of the ear and that of the system of sense-organs usually called the sense-organs of the lateral line, a structure found in Fishes and aquatic Amphibia, larval or adult. Into the differences of opinion and confusion in this field of research Beard,[2] in 1884, introduced a semblance of order, and at the same time gave cause for much further contention, by bringing the two organs, or systems of organs, together phylogenetically, and claiming the ear to be nothing more nor less than a modified portion of the system of the lateral line. Since then much has been written upon this phase of the subject, the chief single contribution, perhaps, being that of Professor Ayers,[3] who adopted and developed very fully the general idea suggested by Beard.

The chief morphological facts upon which this view is based, are, in brief, the following: —

1. *Similarity in ontogeny.* — The ear and the lateral line seem to develop from a common ectodermal thickening, which extends forward and backward from the place of origin.

2. *Similarity in structure of adult organs.* — It is now generally acknowledged by morphologists that the internal ear is not one organ, but a group or system of organs, comprising in the fully developed ear of the fish seven recognizable patches of sensory epithe-

[1] The substance of this article was presented before the Section in Physiology of the British Association for the Advancement of Science at its meeting in Toronto, August 19, 1897.

[2] BEARD, J.: On the segmental sense-organs of the lateral line, and on the morphology of the vertebrate auditory organ. Zool. Anzeiger, 1884, vii, p. 140.

[3] AYERS, H.: Vertebrate cephalogenesis. II. A contribution to the morphology of the vertebrate ear, with a reconsideration of its functions. Journal of morphology, 1892, vi, p. 1.

lium: the three cristæ acusticæ, contained in the walls of the ampullæ of the semicircular canals; the three maculæ acusticæ, contained in the recessus utriculi, sacculus, and lagena; and the rudimentary macula neglecta, contained usually in the utriculus. The structure of these is well known; in each there is a localized area of sensory epithelium, supplied by special nerve-fibres and consisting of hair- and supporting-cells. The processes of the hair-cells project into a liquid, the endolymph. In addition to these parts, common to both cristæ and maculæ, each macula bears a mass of otoliths, resting upon the sensory hairs. The labyrinthine cavity of the internal ear in the Selachians is more or less freely open to the outside medium through the ductus endolymphaticus.

The sense-organs of the lateral line are numerous, and are either free or contained in canals lying in the skin of the head and the sides of the body. These canals are open at intervals directly to the water of the medium, as are the semicircular canals through the endolymphatic duct. From their position, different portions of the lateral system have received the names supraorbital, infraorbital, mandibular, occipital, and lateral. The structure of the sense-organs closely resembles that of the cristæ acusticæ: in each there is a localized area of sensory epithelium, supplied by special nerve-fibres and consisting of hair- and supporting-cells; the processes of the hair-cells project into a liquid which, when canals are absent, is the water of the medium, and, when canals are present, is this water plus more or less mucus excreted by the cells lining the walls of the canals.

3. *Similarity in innervation.* — The sense-organs of the lateral line are innervated by nerve-fibres forming well-marked bundles, which run to the periphery usually in company with branches of the fifth, seventh, ninth, and tenth cranial nerves. To speak of them as being innervated by these cranial nerves is misleading; the connection of their nerves with the cranial nerves is secondary. In reality, the nerves of the lateral line form a definite system of their own with a common central origin, which central origin is, likewise, the central origin of the eighth or acoustic nerve.

It must be acknowledged that these facts are of great importance, and seem to warrant the interpretation given to them.

Can physiology throw any light upon this question? A study of function is not usually believed to be capable of elucidating the genetic relationship of organs, and hence most writers have wholly neglected the physiological side. It might have been advantageous if

more had done this, for the physiology that has thus far been introduced is largely speculative, usually lacks an experimental basis, and is at times grotesque. What is needed here, as in all similar cases, is not speculation from morphological facts as to function and the origin of function, but reasoning from physiological facts that are first acquired by rigid and critical experiment. We have here an admirable opportunity to demonstrate not only that the phylogeny of function is worthy of study for its own sake, but that physiology is at times able to present, if not direct, at least valuable circumstantial evidence of the truth of morphological deductions. The evidence that I wish to bring forward has been obtained, unless otherwise stated, by myself from experiments upon fishes at the Marine Biological Laboratory, Woods Holl, Mass., during recent summers. The form chiefly used was the common smooth dog-fish (Galeus canis, Mitchill) of our Atlantic coast.

Some of the results have already been published, but must be mentioned briefly in this connection for the sake of rendering the subsequent work more easily understood. No attempt will be made to discuss the experiments of others upon higher animals, as this for my present purposes would be quite superfluous. The work is not yet completed.

We will consider the functions of the various sense-organs in order.

I. The Ear.

A. **The cristæ acusticæ.** — The experiments here have been clear-cut, and the results have appeared with a mathematical exactness rarely realized in physiological investigation.

One general function is here present, namely, the appreciation of rotary movements of the body, *i. e.*, movements in curved lines. Hence, the semicircular canals with their sense-organs are organs of equilibration.

The methods of arriving at this conclusion were three: turning the normal fish in the planes of the canals and other planes; stimulating separately and in combination the various ampullar branches of the acoustic nerve, which in the fish are separate and very easily reached; and cutting these ampullar branches. The index to the state of the animal's sense of equilibrium was found in the compensating movements of the eyes and the fins. The results obtained by these three methods are entirely harmonious. Thus, turning the normal

animal in a definite plane, either the plane of a canal or a plane between two canals, causes the eyes and fins to make certain definite and constant movements, which indicate a recognition of the body-movement and an attempt to resist or overcome it. If, now, the canals of the corresponding planes be exposed in another animal, and their cristæ stimulated artificially, exactly the same compensating movements of eyes and fins are made. The inferences are: first, that the operated fish has the sensation of being turned out of his normal position; and second, that when a normal fish turns in the planes specified, he stimulates the corresponding cristæ. This latter inference is corroborated by cutting the nerves supplying the cristæ in question, and then turning the animal in the same planes as before. This has not been done for single cristæ, and it is quite possible that in such case the others would maintain the compensation; but it has been performed for a functional pair of cristæ, and the result is absence of the normal compensating movements pertaining to the canals in question. The harmony of the results of these three methods is striking.

Each canal with its sense-organ has a principal and a subordinate function: the former is the appreciation of rotary body-movements in the plane of the canal and toward its side of the body; the latter is the appreciation of similar movements in the same plane but in the opposite direction. Each canal has a functional opposite, the two lying approximately in the same plane, and the principal function of one being the subordinate function of the other. Such functional opposites are the right anterior and the left posterior, the left anterior and the right posterior, and the right and left horizontal canals. A simple movement of the body in the plane of a canal puts the canal into most complete action; a movement in any other plane may be regarded (from the standpoint of the canals) as a compound movement, and may be resolved into simple movements in the planes of two or more canals. Such compound movements are appreciated by the two or more canals acting as a double organ (functional pair), or triple organ, which likewise possesses its principal and subordinate functions. The action of a functional pair, or double organ, is exemplified in the appreciation of diving movements by the two anterior canals, and in the appreciation of the movement of shooting upward in the water by the two posterior canals.[1]

[1] For a fuller discussion of the functions of the canals the reader is referred to my articles already published. Ueber den Gleichgewichtssinn. Centralbl. f.

B. **The maculæ acusticæ.** — Here not so much work has been done, and the results are not as sharp-cut as in the case of the cristæ. Artificial stimulation of the maculæ has been tried in a large number of cases, but does not appear to give consistent results. Cutting the macular nerves or, perhaps better, removing the otoliths that always cover the maculæ, makes a decided general change in the conduct of the animal, which to one familiar with the movements of fishes seems to indicate unmistakably the lack of certain sensory functions. It should be premised that, in the form studied chiefly, the utricular and saccular maculæ are very closely contiguous, and the macula of the lagena is simply a small continuation of that of the saccule; hence, so far, it has been impossible to separate the three functionally, and it is very questionable whether the division of labor here is as sharp-cut as with the cristæ.

Two functions seem to be present, both of which are equilibrating: the appreciation of translatory or progressive movements, or movements in straight lines, and the appreciation of the position of the body in space.

1. *Appreciation of progressive movements.*[1] — A normal fish has a delicate sense of the distance involved in swimming in a straight line. This is shown by the remarkable skill with which he avoids obstacles; in swimming around his aquarium constantly, he strikes his nose directly against the side of the tank comparatively rarely. This is not so with a fish deprived of all his otoliths or with all his macular nerves severed. Such a fish seems to have little idea of the extent of a forward swim. He is often restless and frequently alters the direction of his progression. In moving along close to the side of a large oblong tank he often swims at his usual rate and with his usual freedom, and appears fairly normal; but, upon reaching the end, it frequently happens that he does not turn, like the normal fish, gracefully to one side and thus avoid the end-wall. On the contrary, he often bumps directly into it. When excited by a stick, he darts about in different directions, irregularly and with awkward,

Physiol., 1892, vi. p. 508. A study of the sense of equilibrium in fishes. Part I. The Journal of physiology, 1893, xv. p. 311; and Part II, *ibid.*, 1894, xvii, p. 192.

[1] A full account of my observations upon this function and upon the subject of hearing in Fishes has not been published. My observations were communicated to The American Physiological Society, 1894, Dec. 28; a brief abstract of that Paper was printed in "Science," 1895, Feb. 1, N. S. i. p. 118, and a still briefer one in the Centralblatt für Physiologie, 1895, April 6, ix. p. 47.

uncertain, and ill-regulated movements, often shooting far out of the water. Moreover, after swimming into a corner, his movements are awkward and he finds great difficulty in retreating or getting back into open water. If he succeeds in doing this, he may return at once to the same corner and repeat his ungainly attempts at extricating himself. It is easy to draw a hasty inference that the eyesight of such a fish must in some mysterious way be at fault. As a matter of fact, however, a fish deprived of his eyesight, but in other respects normal, does not conduct himself in that way. When left to himself, the blinded fish[1] swims normally in all respects, moving gracefully, easily, and without timidity, and shooting and diving like an uninjured fish. When disturbed by being poked he darts about with great rapidity, but is master of his movements. In the first few hours of his blindness he bumps the end of the tank in progressive swimming, but soon he largely overcomes this, and, probably by his sense of touch, learns to avoid gross contact with such obstacles. He then touches the walls lightly, glides away from them easily, and only when disturbed bumps as at first. When by chance he swims into a corner, he extricates himself easily, gracefully, and with certainty. The compensating movements of his eyes and fins are entirely normal.

It is thus seen that the fish deprived of retinal sensations and the fish deprived of macular sensations act very differently. The conclusion that in the latter animal the appreciation of progressive movements is dulled or largely eliminated seems quite sufficient to explain the phenomena.

We thus find experimental proof — and the first thus far reported in animals lower than man, if I am not mistaken — of the presence in the otolithic parts of the ear of a power to appreciate progressive movements. That such a function must exist there was ably advocated by Breuer,[2] who gave reasons for the probability "that the perception of rectilinear movements is sharper in Fishes and Birds than we find it in observations on ourselves."

2. *Appreciation of position in space.* — The fact that a normal fish has a delicate sense of his position in space, of upness and downness, is demonstrated by the difficulty experienced in inducing one to rest

[1] In blinding, the contents of the eyeballs, including the retinas, were removed; the sclerotic coats with their muscular attachments were left *in situ*.

[2] Breuer, J.: Ueber die Function der Otolithen-Apparate. Arch. f. d. ges. Physiol., 1890, xlviii, p. 195.

in any other position than that with the back upward and the belly downward. He not only resists with all his powers being turned over (this movement is appreciated by the semicircular canals), but with equal energy he resists being compelled to remain out of his customary position; and, when put out of the latter and then left to himself, he at once assumes his normal attitude.

It is not so with a fish from which the otoliths have been removed, or in which the macular nerves have been cut. If either of these operations be done upon one side only, the eyes and fins are placed in abnormal positions; in reclining, the operated side is usually slightly downward; normal swimming is possible, but here usually the operated side is depressed; when disturbed, the fish usually darts off with that side downward; and in coming to rest he often loses his balance and sinks down flat upon that side, never upon the other. If the operation be performed on both sides, the fish seems to have largely lost his sense of upness and downness. While preferring usually the normal attitude, it is not difficult to make him remain lying on his back or side; and not rarely he is found in such abnormal positions, having assumed them himself. He swims at times upon his side, and occasionally upon his back. He seems not to appreciate at all clearly his position in space.[1]

I have found no reason to disbelieve that the same otolithic parts of the ear appreciate both progressive movements and position in space, which is not in accordance with the doctrine of specific energy in its extreme form. The view of Breuer,[2] however, seems wholly reasonable, namely, that changes in the pressure of the otoliths are appreciated as changes of position in space when they are accompanied by sensations (ampullar) of rotary movements, and as progressive movements when not so accompanied.

It is evident that there is a close functional connection, through the central nervous system, between the sensory organs of the ear, the cristæ and maculæ, and the locomotor organs of the body. A reflex arc with the evident function of equilibration is thus established. The idea that the cristæ and maculæ are sensory organs of this function does not preclude acceptance of the well-established fact that other

[1] For a fuller discussion of this statical function of the maculæ, the reader is referred to the author's articles in the Centralblatt für Physiologie, 1892, vi, p. 508, and the Journal of physiology, 1893, xv, p. 311.

[2] BREUER, *loc. cit.*

sensory organs, such as the eyes, are similarly connected by reflex arcs with the locomotor organs, and similarly functionate as sensory organs of equilibration. In these latter organs equilibration is accessory to other chief functions, as in the eyes to sight; in the cristæ and maculæ it is the chief, and perhaps the only, function.

The functions of the ear of the fish so far considered may be put in convenient tabular form as follows:—

I. Dynamical functions, in recognition of	1. Rotary movements, mediated by cristæ acusticæ.
	2. Translatory movements, mediated by maculæ acusticæ.
II. Statical functions, in recognition of	3. Position in space, mediated by maculæ acusticæ.

As to the manner of stimulation, it is evident that both the cristæ and the maculæ belong to the category of pressure-organs. This is most evident in the maculæ, in which the pressure of the otolithic mass upon the delicate sensory hairs affords a constant stimulus which varies in intensity with the position of the animal in space, or with the force of the progressive movement.

In the cristæ, the most reasonable mode of stimulation appears to me to be that due to the inertia of the endolymph as the hair-cells are moved through space along with the body. The result is a greater pressure upon one side of the hairs than upon the other, and hence a stimulation of the sensory cells by pressure.[1]

[1] In a recent article E. v. Cyon (Bogengänge und Raumsinn. Experimentelle und kritische Untersuchung. Archiv fur Physiologie, 1897, p. 29) appears in the light of a sceptic regarding the results obtained in my experiments on dog-fishes, apparently because of their exactness and completeness. Among other things he reproaches me with the fact that "Lee hat . . . immer alles bestatigt gefunden, was die Hypothese erheischt." This fact will occasion no surprise, when it is borne in mind that the great majority of my results were obtained long before the "hypothesis" as formulated by myself was made (cf. LEE: Journ. of physiol., 1893, xv. p. 321), and long before I was acquainted with the work of Breuer. The theory as formulated in my chief Paper was a direct induction from the facts obtained by myself; I took pains to keep it within the limits of those facts, and thus it was that I "always found what the hypothesis demanded." In a subsequent Paper (LEE: *ibid.*, 1894, xvii. p. 192) I aimed "to fill in certain gaps that were left in the previous series, to make the proof of certain points more logically complete, and experimentally to verify certain inferences and prophecies resulting from the theory formerly stated." As regards the exactness of my results, I have often felt and expressed surprise similar to that which Cyon apparently feels. Yet I have endeavored accurately to chronicle the phenomena

C. **The question of hearing.** — We thus appear to have found a function for all of the sensory organs of the ear of the fish. But the question naturally arises — does not the fish possess audition? In higher vertebrates, of course, this is present, and we can add to the above scheme:

III. Auditory functions, in recogniton of { 4. Vibratory motions, mediated by papilla acustica basilaris.

This exhausts all possible cases of mechanical (*i. e.* visible) motions in matter. It is interesting that the ear is the sense-organ that appreciates all kinds of visible motion.

Wherever among vertebrates undoubted audition exists, there is present an additional group of sensory end-organs, the papilla acustica basilaris. This does not exist in Fishes, but appears first in the Amphibia as an offshoot from the lagena, and in higher vertebrates constitutes the nervous portion of the organ of Corti of the cochlea.

actually observed under the circumstances of the many and widely varied experiments.

Cyon further seems to regard the integrity of the sense of sight as necessary to the performance of the compensating movements of the eyes, and makes the astonishing statement that ". . . der Dogfish (Galea canis) tagesblind ist, wie Beer unzweifelhaft bewiesen hat." On the contrary, Beer (Die Accommodation des Fischauges. Arch. f. d. ges. Physiol., 1894, lviii, p. 577) has neither stated nor attempted to prove such a thing. He says: "Wir haben einigen Grund anzunehmen, dass die Pupille der in Freiheit lebenden Fische wegen der relativen Dunkelheit grösserer Tiefen noch etwas weiter sein wird, als bei den Thieren in den gewöhnlichen Versuchsbassins, die in einer für sie vielleicht blendenden Helle leben. Bei vielen Haifischen und Rochen tritt sogar in den dunkleren grossen Aquarien der Station tagsüber eine so starke Miosis ein, dass die Pupille — die Nachts, resp. im Dunkeln sehr weit ist und dann auch hier den Linsenrand sehen lässt — fast gar nicht sichtbar, sondern . . . verschlossen wird; die Thiere benehmen sich auch wie blind," etc. As a matter of fact, under the circumstances of my experiments, the pupils of Galeus canis varied greatly in size, from being wide open to being partially closed. But I do not now recall a single instance of their being wholly closed, nor have I ever seen an uninjured individual of this species behaving during the daytime like a blind fish. In an experience of three summers this species has not exhibited himself as "blind in daylight." This question is, however, of minor importance, since, as stated above, the eyeballs from which the contents, including the retinas, are removed, perform the normal compensating movements. Cyon appears not to comprehend the fact accented above, namely, that the movements of the eyes are reflex movements, the afferent stimulus to which comes from the cristæ acusticæ. This does not preclude the further undoubted fact that under normal circumstances the movements are accompanied by sensations of sight.

At first sight the presence of the "ear" in Fishes presupposes a sense of hearing; but the absence of the papilla acustica basilaris argues against it. The fact that fishes, with comparatively few exceptions, are dumb seems to me strong evidence against the possession by them of a sense of audition. It would seem that the primary purpose of the power of emitting sound by an organism is communication with other individuals of its own species. Similarly, the primary purpose of a sense of hearing is apparently the gaining of information regarding the presence of other individuals of one's own species. In each case the employment of the function for other purposes would be secondary. If this be so, we should expect the two powers of emitting sound and of hearing sound to be developed in the same individuals and developed more or less *pari passu*. A survey of the various groups of animals shows this to be the case. Further, it is difficult to conceive upon any grounds the object or usefulness of the possession by Fishes of the power to hear in the sense in which the term is ordinarily used. The depths of the sea are silent, the sounds of the waves probably penetrate only the most superficial layers of the water, and aquatic animals, with comparatively few exceptions, are dumb. Along the shores some outside sounds might penetrate the water superficially, but such would form only a very slight exception to the general law that in nature water, unlike air, is devoid of sound.

But experimentation can best answer the question as to the power of audition in Fishes.

In the summer of 1894 I tested a number of species as to their power of hearing, employing ordinary sounds, such as the human voice, clapping the hands, and striking stones together in the air and under water.[1] I obtained no evidence whatever of the existence of a sense of hearing as the term is customarily employed, although I learned that fishes are exceedingly sensitive to gross shocks, such as the jarring of their tank or concussions upon its walls, *i. e.*, such vibrations as human beings recognize through other sensory mechanisms than the ear as distinct mechanical vibrations. The accompaniment of such apparently gross vibrations was the indispensable condition upon which the fishes in my experiments reacted to sounds. I have learned recently of Bateson's similar experiments[2] which were

[1] See footnote p. 132.

[2] BATESON, W.: The sense-organs and perceptions of fishes. Journal of the marine biological association, 1890, i, p. 225.

interpreted in much the same way. In 1895 Kreidl[1] published the results of a considerable series of experiments carefully conducted upon goldfish. He used as sources of sound in the air various whistles, electric and other bells, clapping of the hands, and the firing of a revolver, and in the water vibrating rods; and he studied their effects upon normal fishes, those whose excitability was greatly increased by strychnine, and those that had been deprived of their ears. Neither normal nor strychnized fishes showed any reaction whatever to musical sounds of any pitch or intensity, produced in the air or water. Concussions, such as striking the walls of the aquarium in the case of normal animals, or clapping the hands or firing a revolver in the case of strychnized animals, produced marked reactions, especially in the latter; but such reactions were equally well-marked after both ears were removed, and still remained after the removal of the whole cerebrum and a portion of the mid-brain. His experiments leave no doubt of the correctness of his conclusions, which were: "(1) That hearing through the 'auditory organ' cannot be demonstrated in the goldfish; (2) nevertheless, they react to sound waves, which they perceive through a specially developed skin-sense."

In a subsequent paper Kreidl[2] explodes the oft-repeated tale of hearing by fishes that come for their food at the sound of a bell, by investigating carefully the actions of trout at the famous old Benedictine monastery in Krems, Austria. He proved that the fishes come because they see the man who brings the food, and appreciate the vibrations of the water caused by his step and communicated through the stone basin; and that, when these are excluded, the sounds of the bell have no effect.

The conclusion seems justified beyond doubt that fishes do not possess the power of hearing, in the sense in which the term is ordinarily used.

We must believe that in vertebrates this sense was evolved along with a change of the mode of life from a water to a land existence, and was contemporaneous with the appearance of a papilla acustica basilaris.

It appears plain that the sole function of the ear in Fishes is equilibration.

[1] KREIDL, A.: Ueber die Schallperception der Fische. Arch. f. d. ges. Physiol., 1895, lxi, p. 450.

[2] KREIDL, A.: Ein weiterer Versuch über das angebliche Hören eines Glockenzeichens durch die Fische. Arch. f. d. ges. Physiol., 1896, lxiii, p. 581.

The mechanism by which Fishes appreciate certain mechanical vibrations and which Kreidl proved not to reside in the ear, is no more understood in them than it is in other animals and in human beings. This power is wide-spread in animals, even in many Invertebrates in which there is an absence of the power of hearing, *e. g.*, in earthworms, and it is astonishingly developed in some human beings. My friend, Professor Hallock, tells me that Helen Keller, who, it is well known, is totally deaf and devoid of other special senses except that of touch, is able, by keeping her fingers in contact with the larynx of a person who is singing, to appreciate accurately the changes in pitch; she can thus accurately reproduce with her own voice the notes sung by her companion. There is no question here of the absence of the sense of hearing, yet the vibrations are appreciated. As regards these two sense-activities, the case of the normal fish is without doubt analogous to the case of such defective human beings.

II. The Lateral Line.

The original view of the function of the lateral line was that its canal produced mucus for moistening the surface of the body of the fish. When in 1850 Leydig[1] discovered the numerous sense-organs in it and later ascribed to them the mediation of a sixth sense, the original view was laid aside for others of a sensory function. Upon little experimental evidence it has been suggested that the organs are true touch-organs, are auditory organs, that they appreciate currents in the surrounding water, the chemical nature of the water, and so on. There has been no consensus of opinion as to their exact function or mode of action.

During the summers of 1892, 1893, and 1894, I carried on at different times experiments of various kinds upon the lateral-line system (not including the ampullæ of Lorenzini or Savi's vesicles). I studied several species of fishes, especially the dog-fish (Galeus canis, Mitchill), the toad-fish (Batrachus tau, L.), and the butter-fish (Stromateus triacanthus, Peck), and obtained certain suggestive results. The main points will be communicated here.

In the dog-fish the lateral-line organs of the head are supplied by the superficial ophthalmic, the buccal, and the hyomandibular branches of the seventh nerve; those of the body by the so-called lateral branch of the vagus. In this species I have cut all of these

[1] Leydig, F.: Ueber die Schleimkanale der Knochenfische. Muller's Arch., 1850, p. 170.

branches, and, moreover, have stimulated the central end of the lateral branch. In the toad-fish, where the organs are normally exposed and not enclosed in canals, I have destroyed by thermo-cautery all of the organs upon one and upon both sides of the body. In general, it may be stated that the results indicate that the organs of the lateral line have a sensory function, closely connected with the motor organs and analogous to the functions of the ear, and hence may be regarded as organs of equilibrium.

Simple cutting of the lateral nerve on one side or even both sides, cutting of all the nerves supplying the lateral-line organs of both head and body, or destruction of all the organs themselves, does not seem to interfere much, if any, with the animal's equilibrium. I have observed at times an abnormally slow return to the normal position after an animal so operated upon has been turned upon his back, but whether this was due to dulling of a sense of equilibrium or to general weakness, I am unable to say. All these experiments were performed more than five years ago, however, and before experience had taught me to observe and interpret interferences with equilibrium, hence I would not now be willing to make a categorical statement regarding the effects of operations of this kind. The animals so operated upon are always much less active than before; they swim little, lie quiet, and rarely survive more than a day or two at most.

An extension of such operations has given more decided results. It occurred to me that a reduction of the motor mechanism employed in maintaining equilibrium might be an indirect aid in demonstrating a possible equilibrium function in the lateral-line organs. In the toad-fish, which spends much of its time lying upon the bottom of the sea, especially in holes under stones, the pectoral fins are enormously developed and seem to act as mechanical supports. Removal of these fins does not, however, of itself cause marked inconvenience in the maintenance of statical equilibrium or the performance of movements; the subsequent removal of the two smaller ventral fins is followed by no apparent genuine lack of the power to appreciate equilibrium and only a comparatively slight handicapping of the power of movement. It is remarkable how closely the actions of a fish deprived of these four fins resemble those of a normal fish; he is lively, vicious, quick in responding to mechanical stimuli, and certain in his movements; he guides himself accurately, turns about suddenly, and moves forward without lateral swaying of his body. But removal of the four fins combined with destruction of all the

organs of the lateral line (except the supraorbital ones, which are few in number and lie too deep for ready operation), produces a marked effect. This has been performed in several individuals. No genuine forced movements seem to follow, but there are decided evidences of a lack of the sense of equilibrium. This is manifested in various ways. There is decided uncertainty in movement, the animal swaying from side to side in forward progression. Such a fish is easily turned upon his side or back and lies quiet in this position. In one case, some two hours after the operation, the toad-fish was turned upon his back upon the bottom of his aquarium and remained thus for fifteen minutes, apparently without discomfort, and without attempting to return to the customary position. He was then returned to the latter by the hand. Such a fish swims irregularly upon his back or his side, with a general preference for the normal attitude. In one case in which the lateral organs of one side only were destroyed, and the pectoral and pelvic fins were removed, the power of maintaining equilibrium was found to be markedly weakened. When tested five hours after the operation, and presumably after the direct shock of it had passed away, the fish lay on his back when placed there; in swimming upward he thrust his head far out of water in much the same way as a fish deprived of his otolithic organs; and he showed the lateral swaying movements and uncertainty in forward progression, mentioned above. On the next day he exhibited the same phenomena. All the actions of a fish so operated upon remind one much of a lobster that has lost his otolithic sacs and chelæ.[1] The phenomena indicate strongly that the organs of the lateral line have something to do with equilibrium. In this connection it is of interest to know that Bonnier[2] has recently found that fishes whose lateral organs have been destroyed by galvano-cautery have largely lost the capacity of correct orientation in presence of disturbances in water.

It might be objected that the severity of the operation of cauterizing so many spots in the skin and removing the four fins might of itself be the cause of the disturbances of equilibrium above described. I have anticipated and nullified the possible force of such an objection by cauterizing an equal number of spots upon the skin of a nor-

[1] Bunting, M.: Ueber die Bedeutung der Otolithenorgane fur die geotropischen Function von Astacus fluviatilis. Arch. f. d. ges. Physiol., 1893, liv, p. 531.

[2] Bonnier, P.: Sur le sens lateral. Comptes rendus de la soc. de biol., Paris, 1896, p. 917.

mal fish, carefully avoiding the lateral line, and then removing the four fins. Such an animal does not behave differently from one lacking the fins and not otherwise injured; he is active and certain in his movements, shows no lack of equilibrium, and in general closely resembles a normal fish.

But perhaps more significant than the above experiments on elimination is the result of stimulating the central end of the lateral nerve. In the dog-fish I have cut the nerve upon one side and stimulated it by an induced current just behind the head, thus including the nervous supply of all the organs of that side of the trunk. The result is perfectly coördinated, definite movements of the fins of both sides of the body. These fin-movements are the same as those called out by stimulating centrally the cut acoustic of the opposite side, and the same as those resulting from section of the acoustic of the same side. Thus, stimulating the left lateral nerve centrally caused: the two dorsal fins to move to the right; the caudal fin to move to the right; the left pectoral fin to move upward; the right pectoral fin to move downward; the two pelvic fins to move like the corresponding pectorals. This is exactly the result of stimulating the central stump of the right acoustic,[1] and also the exact result of cutting the left acoustic.[2] In the case of the acoustic I have shown that the result of stimulation is only what would be expected from a simultaneous and equal stimulation of the three ampullar branches of the acoustic. Since these branches are plainly equilibrative in function, it would seem to suggest strongly that the lateral nerve is also equilibrative. Occasionally, movements of the fins in directions opposite to those specified above take place, but they are by no means so constant or persistent, and, thus far, I have not attempted to determine the conditions of their appearance. In this connection it may be recalled that moderate or strong stimulation of the ampullæ of the semicircular canals causes movements of the eyes in a certain direction (principal function), and slight stimulation causes movements in exactly the opposite direction (subordinate function).[1] Movements of the trunk also result from stimulation of the lateral nerve, but thus far I have not endeavored to analyze them.

This is the extent of the experimenting that I have performed upon the lateral line, but, so far as it goes, it seems very suggestive. It would be interesting to test the lateral nerve at different parts of its course, and observe whether movements of the fins of different

[1] LEE: Journ. of physiol., 1894, xvii, p. 192. [2] *Ibid*, 1893, xv, p. 311.

segments result. Further, I have observed no eye-movements from lateral stimulation. It is conceivable that eye-movements may be mediated by the lateral-line organs of the head only, but so far I have not tested this possibility by stimulating the branches of the seventh nerve.

Without further work, which is already projected, it is impossible to specify in detail the nature of this possible equilibrative function of the sense-organs of the lateral line. The phenomena suggest Schulze's [1] idea of the possibility of appreciation of mass-movements of the water or of movements of the body through the water, just as the movements of the hairs of the cristæ through the inert endolymph mediate the appreciation of rotary movements of the body. Such a function seems more easily understood in the case of those fishes, such as the toad-fish, in which the sense-organs project freely to the outside, than in those in which the organs are enclosed within canals that open to the outside only at intervals. Yet in all species such a function seems to me *a priori* the most probable of all that have been suggested. The appreciation of rotary movements and that of progressive movements can hardly be separated here. It is not inconceivable nor improbable that, in addition to this function, contact with solid objects, such as the sand and stones at the bottom of the sea, may stimulate the organs and assist crudely in giving the fish a notion of his position in space. The structure of the organs suggests, as in the sense-organs of the ear, that they are pressure-organs of some kind. In this connection the work of Fuchs [2] is interesting. This investigator has shown by experiments upon Raja clavata and Raja asterias that touching the skin over the ventral canals of the head causes in most cases a negative variation of the current of rest in the cut nerves supplying these canals. He infers, not wholly with justification it seems to me, that the canals mediate the appreciation of changes of hydrostatic pressure.

In whatever specific way future experiments may prove the sense-organs in question to act, it is at least clear that those of the trunk are connected through the central nervous system with the muscles of the fins, and that a reflex arc is thus present, analogous in nature to that formed by the same motor mechanism with the acoustic nerve.

[1] Schulze, F. E.: Ueber die Sinnesorgane der Seitenlinie bei Fischen und Amphibien. Arch. f. mikr. Anat., 1870, vi, p. 62.

[2] Fuchs, S.: Ueber der unter der Haut liegenden Canalsysteme bei den Selachiern. Arch. f. d. ges. Physiol., 1895, lix, p. 454.

We must believe, moreover, that the impulses of whatever kind that come to the central nervous system from the organs in question assist in enabling the animal to maintain the equilibrium of his body: in other words, the organs of the lateral line are equilibrating organs.

Hence, a consideration of the physiology of the ear and the system of the lateral line, by showing that the two systems of organs are functionally analogous, would seem to offer indirect support to the morphological deduction that the former organ is a derivative of the latter. The primitive function, not improbably, was the appreciation of movements of the water against the body and movements of the body in the water, combined with appreciation of contact, and, hence, indirectly and crudely, of position in space; by the exercise of this function, through functional connection with the locomotor mechanism, the equilibrium of the body was maintained. In some unknown way a bit of this sensory system became cut off from the rest and enclosed within the skull; it still retained its power of appreciating bodily movements and contact, and this power became refined and differentiated; the capacity of appreciating rotary movements was separated from that dealing with progressive movements and position in space, and the two were associated with distinct organs, the semicircular canals on the one hand, and the otolithic organs on the other, which were appropriately constructed to subserve their respective functions. Thus a well-marked sensory organ for equilibrium was evolved in fishes. When aquatic animals began to leave the water and live for a shorter or longer time upon the land, and the possible advantage of a sense of hearing was presented, a portion of this sensory organ of movement became still farther differentiated; a new patch of sensory nerve-terminations appeared, the papilla acustica basilaris; apparatus for conveying the waves in the air directly to the membranous ear was developed; and thus the power of appreciating the movements that we call sound was acquired. By natural selection this was still more refined and specialized, the range of appreciation was extended, and the result is the mammalian cochlea with its great functional powers.

It seems to me that this explains naturally and in a manner not improbable the mysterious association in one organ of two functions at first sight so widely separated as equilibration and audition.